

*Appeal No. 14-1020(L)
14-1033(XAP), 14-1039(XAP)*

IN THE
United States Court of Appeals
FOR THE FEDERAL CIRCUIT

JARROW FORMULAS, INC.,

Plaintiff-Appellant,

v.

NOW HEALTH GROUP, INC. DBA Now Foods,

Defendant-Cross Appellant.

SOFT GEL TECHNOLOGIES, INC.,

Plaintiff/Counterclaim Defendant-Cross Appellant,

v.

JARROW FORMULAS, INC.,

Defendant/Counterclaimant-Appellant.

*On Appeal from the United States District Court for the Central District
of California in Case Nos. 2:10-CV-08301-PSG-JC and 2:11-CV-00164-PSG-JC,
Honorable Philip S. Gutierrez*

**NON-CONFIDENTIAL OPENING BRIEF
FOR PLAINTIFF-APPELLANT/
DEFENDANT/COUNTERCLAIMANT-APPELLANT**

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1. The full names of every party or amicus represented by the undersigned are:

Jarrow Formulas, Inc.

2. The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by the undersigned is:

None

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by the undersigned are:

None

4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by the undersigned in the trial court or agency or are expected to appear in this court are:

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The material redacted from this brief is subject to a protective order. The information redacted on pages iii, iv, 13, 14, 15, 16, 17, 18, 19, 21, 22, 23, 29, 30, 31, 32, 34, 48 relates to documents that have been designated as confidential pursuant to the protective order and contains confidential information belonging to defendants-cross appellants, including trade secret technical information that is not publicly available.

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ABBREVIATIONS AND CITATIONS

Parties:

Jarrow	Plaintiff/Declaratory Judgment Defendant - Appellant Jarrow Formulas, Inc.
NOW	Defendant - Cross Appellant Now Health Group, Inc. DBA Now Foods
Soft Gel	Declaratory Judgment Plaintiff - Cross Appellant Soft Gel Technologies, Inc.

Defined Terms:

‘786 patent	United States Patent No. 7,588,786 B2
Accused Supplements	Dietary supplements sold by Soft Gel under the trademarks CoQsol-CF, CoQsol-CF Translucent, and CoQH-CF, and sold by NOW under the trademarks CoQsol-CF and CoQH-CF
CoQ ₁₀	Coenzyme Q10
May 4 Declaration	Declaration of Robert O. Williams, III, dated May 4, 2012
May 25 Declaration	Declaration of Robert O. Williams, III, dated May 25, 2012
Nazzal	Dr. Sami Nazzal, one of the co-inventors of the ‘786 patent
Nazzal Declaration	Declaration of Sami Nazzal, dated May 4, 2012
PTO	United States Patent & Trademark Office

Williams or
Dr. Williams Dr. Robert O. Williams, III, Jarrow’s disclosed technical expert

Williams
Declarations The May 4 and May 25 Declarations, collectively

Citations:

A_____ Citation to Addendum and Joint Appendix

Note: Citations to patents identify column number and line number and are designated as: A____,column number:line numbers.
Example: A0100,17:21-26.

Citations to declarations and expert reports identify paragraph number and are designated as: A____,¶____.
Example: A0200,¶8.

Citations to deposition transcripts identify page and line number and are designated as: (A____,page number:line numbers.)
Example: A0300,23:24-28.

STATEMENT OF RELATED CASES

No other appeals in or from the same civil actions or proceedings in the lower court were previously before this or any other appellate court. There are no cases known to counsel to be pending in this or any other court that will directly affect or be directly affected by this Court's decision in the pending appeals.

JURISDICTIONAL STATEMENT

The District Court had original jurisdiction over the consolidated cases for patent infringement, invalidity and declaratory relief pursuant to 28 U.S.C. § 1338(a), 28 U.S.C. § 2201, and 28 U.S.C. § 2202.

The District Court entered a final judgment in the consolidated cases on September 9, 2013. A Notice of Appeal was timely filed by Jarrow Formulas, Inc. on October 8, 2013. A Notice of Appeal was timely filed by Soft Gel Technologies, Inc. on October 17, 2013. A Notice of Appeal was timely filed by NOW Health Group, Inc. DBA NOW Foods on October 21, 2013. This Court has appellate jurisdiction pursuant to 28 U.S.C. § 1291.

THE ISSUES PRESENTED FOR REVIEW

1. Whether the District Court erred in finding that no genuine issue of material fact existed as to whether the Accused Supplements include a sufficient amount of volatile essential oil to reduce the melting point of ubiquinone to 37°C or below.

2. Whether the District Court abused its discretion by excluding the declarations of Jarrow's technical expert where the declarations explained the expert's previously disclosed opinion and rebutted criticism of his opinion?

3. Whether the District Court abused its discretion by excluding, as undisclosed expert opinion, the factual declaration of one of the inventors describing his personal knowledge regarding the development and application of his own invention?

STATEMENT OF THE CASE

I. PROCEDURAL HISTORY

By way of its Second Amended Complaint, filed on January 12, 2012, Jarrow asserts that NOW infringed the ‘786 patent. (A243-72).

By way of its First Amended Complaint, filed on September 16, 2011, Soft Gel asserts that it is entitled to a declaratory judgment that the ‘786 patent was not infringed, is invalid, and that Jarrow engaged in inequitable conduct in its procurement. (A164-95). By way of counterclaims filed on October 3, 2011, Jarrow asserts that Soft Gel infringed and willfully infringed the ‘786 patent and that Jarrow is entitled to injunctive relief. (A196-242).

On May 2, 2011, the District Court entered an order consolidating the two actions and administratively closing the action filed by Soft Gel.

A. Claim Construction and Summary Judgment of Non-Infringement

On July 31, 2012, the District Court held a hearing on claim construction and the parties’ cross-motions for summary judgment. On August 2, 2012, the District Court entered its Order CONSTRUING CLAIMS and GRANTING Defendants’ Motion for Summary Judgment. (A8-35)¹. In its ruling on claim construction, the District Court concluded that: 1) the preamble term “Eutectic-Based Delivery System” does not limit the claims, A13-16; and 2) the term

¹ The Order is reported at 2012 WL 3186576 and 2012 U.S. Dist. LEXIS 113192.

“melting point” means “the temperature at which a chemical agent has a transition from solid to liquid due to the application of heat”, A16-21.

In its rulings on summary judgment, A21-30, the District Court granted summary judgment to Soft Gel and NOW on Jarrow’s infringement claims, concluding that the evidence submitted by Jarrow “prior to May 4 provides no basis from which a jury could conclude that the CoQ10 in the Accused Supplements is liquid at or below 37[°]C due to a change in its physical properties, *i.e.*, a reduction in its melting point.” (A30).

In rendering its summary judgment rulings, the District Court refused to consider several documents submitted by Jarrow on or after May 4, 2012. First, the District Court struck the May 4 and May 25 Declarations. (A614-705, A1215-45). The District Court concluded that these declarations were improper supplemental reports under Fed. R. Civ. P. 26(e). (A27-A29). Second, the District Court struck the Nazzal Declaration. (A706-A726). The District Court concluded that the Nazzal Declaration contained expert opinions which were not the subject of a prior expert disclosure. Without identifying which portions of the Nazzal Declaration constituted expert opinion, the District Court ordered that “all expert testimony proffered by Dr. Nazzal is hereby STRICKEN as untimely.” (A29 (emphasis in original)).

B. Bench Trial on Inequitable Conduct

On March 12 and 13 and June 13, 2013, the District Court conducted a bench trial on Soft Gel's inequitable conduct claim. On August 23, 2013, the District Court issued its Findings of Fact and Conclusions of Law Following Bench Trial. (A36-A48). The District Court concluded that Soft Gel failed to prove that Jarrow engaged in inequitable conduct before the PTO. (A48).

On September 9, 2013, the District Court entered a final judgment: (i) in favor of Soft Gel and NOW on infringement; (ii) in favor of Jarrow on inequitable conduct; and (iii) dismissing without prejudice and as moot Soft Gel's invalidity claim. (A1-7).

II. THE '786 PATENT, JARROW, AND COQ₁₀

The '786 patent is directed to an orally administered dietary supplement comprising CoQ₁₀ and a sufficient amount of a volatile essential oil to reduce the melting point of CoQ₁₀ to 37°C or below and thereby solubilize the CoQ₁₀ at or below body temperature. (A71,19:28-20:40). CoQ₁₀ is also referred to as "ubiquinone" and these terms are used interchangeably in the '786 patent.² (A62,1:31-32; 2:47-49).

² Jarrow's expert, Dr. Williams, opined that "the person of skill in the art at the time of invention would have understood that ubiquinone or CoQ10 was also known and referred to, interchangeably, as ubidecarenone, CoenzymeQ, CoQ, Q10 and/or Q." (A380,n.4). Soft Gel agrees: "The patent is clear that CoQ10 is short hand for ubiquinone and coenzyme Q10..." (A1001,lines 6-7).

Jarrow is a manufacturer of dietary supplements headquartered in Los Angeles, California. (A8; A113, ¶4; A1061). The ‘786 patent issued to Jarrow on September 15, 2009. (A49). Drs. Khan and Nazzal, the inventors of the ‘786 patent, developed their invention at Texas Tech University. (A37). Jarrow acquired the ‘786 invention through an assignment from Texas Tech. (A39-40).

Jarrow sells CoQ₁₀ under the brands Q-Absorb[®] and QH-Absorb[®], and is a leading supplier of such products. (A1061; A1063). CoQ₁₀ “is a lipid-soluble antioxidant found in every cell in the body,” and “is an important component of the mitochondrial respiratory chain.” (A765-772; A62,1:31-33). CoQ₁₀ supports heart function as a component of the electron transport system needed for energy production within the cells, and as an antioxidant protects mitochondrial membranes and cholesterol from oxidation. (A1061; A741, A766-68). In view of these functions, “CoQ₁₀ can lower blood pressure, enhance cardiac function in patients with cardiomyopathy, improve symptoms of congestive heart failure, relieve angina, and increase recovery from heart attack. Additionally, it may slow the progression and improve the symptoms of neurodegenerative diseases, such as Parkinson’s disease.” (A741). In order to achieve these benefits, CoQ₁₀ must be effectively absorbed into the bloodstream. (*Id.*)

III. THE PROBLEM OF POOR ABSORPTION AND BIOAVAILABILITY OF COQ₁₀

Soft Gel describes the “absorption dilemma” of CoQ₁₀ as follows (A741):

The CoQ₁₀ Absorption Dilemma

In order to be absorbed, all nutrients must first be in a water-soluble form. Unfortunately, because of its structure, CoQ₁₀ is highly lipophilic (fat-loving) — and practically insoluble in water. This lipophilic nature makes CoQ₁₀'s absorption:

- **Poor:** Less than 6% of orally administered CoQ₁₀ permeates the gastro-intestinal tract into the blood.
- **Highly variable:** Some individuals absorb considerably less CoQ₁₀ than others.
- **Strongly dependent on stomach contents:** Foods rich in fat enhance absorption.

Making matters worse, CoQ₁₀ is a **large molecule**, contributing to its poor absorption. Plus, when CoQ₁₀ is produced commercially crystals are formed that melt when they reach 118°F or 48°C. Upon cooling, CoQ₁₀ recrystallizes, which frequently results in even **larger crystals** — and further lowers CoQ₁₀ bioavailability.

IV. THE '786 INVENTION OVERCOMES THE ABSORPTION DILEMMA OF COQ₁₀

The inventors of the '786 patent made the discovery that a sufficient amount of volatile essential oil reduces the melting point of CoQ₁₀ to 37°C or below to thereby solubilize the CoQ₁₀ at or below body temperature. (A71,6:36-40,19:28-36). As a result, the "absorption dilemma" is overcome by mixing CoQ₁₀ with a sufficient amount of volatile essential oil. (A65,7:48-51; A379-81,¶¶18-20).

The depression of CoQ₁₀'s melting temperature is significant because human body temperature is typically about 37°C (range (oral) 33.2-38.1°C, mean 36.2°C). (A381,¶20). Thus, depression of the melting temperature means that higher

amounts of CoQ₁₀ can be solubilized, and remain solubilized, without requiring heating to high temperatures. (*Id.*; A64-65,6:57–7:2). The reduction in melting point prevents crystals from forming, and if they do form, causes the crystals to melt when subjected to body temperature. (A381,¶20; A65,7:48-51). The elimination of crystals allows better absorption into the bloodstream and, in turn, enhances the beneficial effect of the dietary supplement. (A381,¶20; A740-47). Accordingly, the increased solubility of CoQ₁₀ improves its overall bioavailability, and means that less CoQ₁₀ must be administered in order to achieve a desired systemic concentration. (A381,¶20; A743-44; A754-59).

V. THE ‘786 PATENT DISCLOSES THE INVENTORS’ TEST DATA DETAILING THE RATIOS OF COQ₁₀:OIL REQUIRED TO REDUCE THE MELTING POINT OF COQ₁₀ FOR A VARIETY OF VOLATILE ESSENTIAL OILS

FIGS. 1-4 of the ‘786 patent illustrate the inventors’ test data demonstrating the reduction in melting point of CoQ₁₀ when mixed with sufficient amounts of different volatile essential oils. (A50-52; A63,3:29-37; A64,5:45-6:40). FIGS. 1 and 3 are Differential Scanning Calorimetry (“DSC”) thermograms generated using a differential scanning calorimeter. (A63,3:29-35).

As reflected in the DSC thermograms, each test sample was a mixture of CoQ₁₀ and a volatile essential oil defining a ratio of CoQ₁₀:oil. Different ratios of CoQ₁₀ to essential oil between 80:20 and 20:80 (w/w) were prepared and subjected

to DSC thermal analysis carried out between 25°C and 60°C at a heating rate of 10°C per minute. (A64,5:61-6:40).

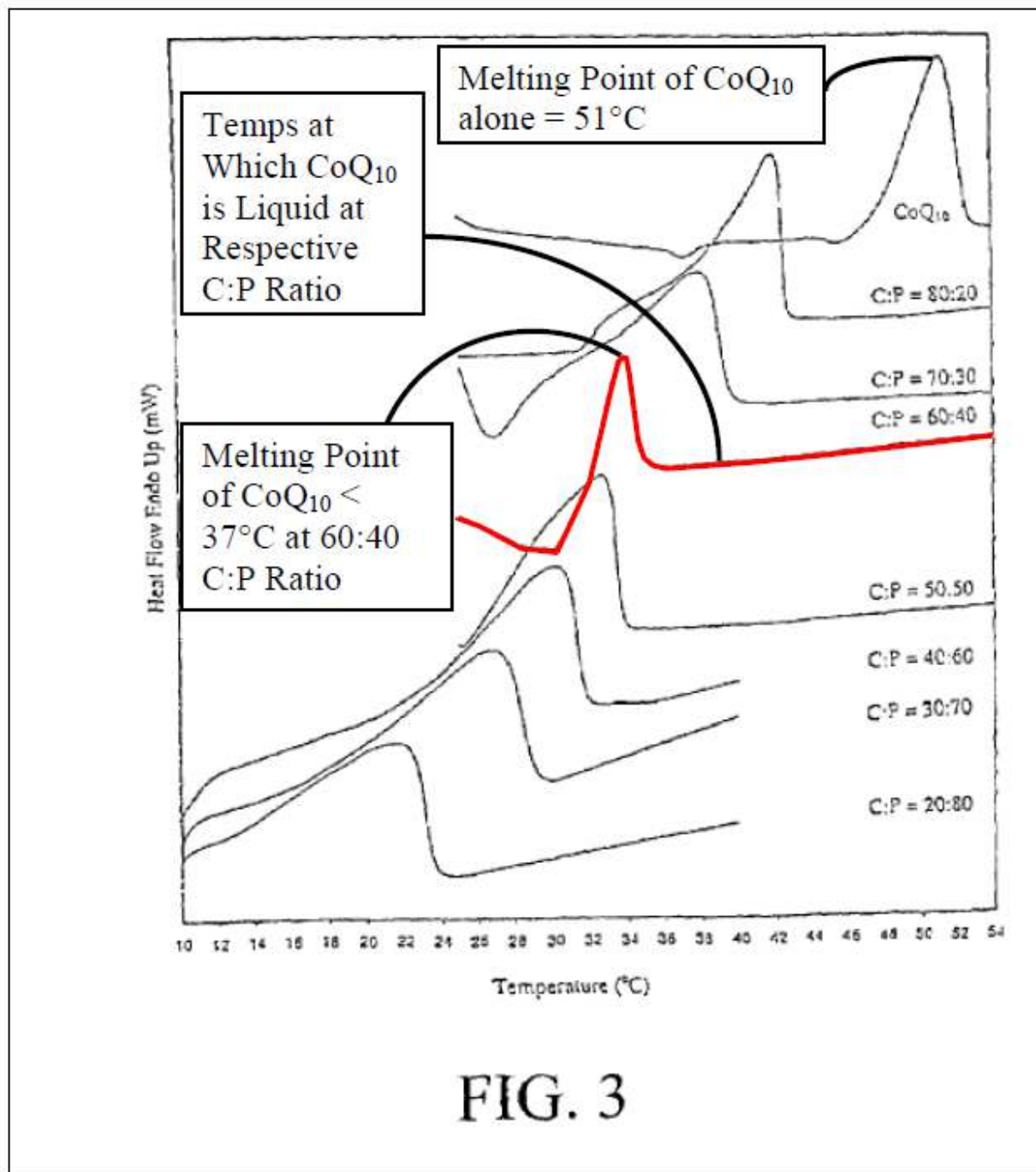


FIG. 3 (A51, reproduced above with text boxes and highlighting added) shows representative melting point data for combinations of CoQ₁₀ and peppermint

The same DSC procedure as outlined above for peppermint oil, and represented by FIG. 3, was performed for a variety of other volatile essential oils including spearmint oil, lemon oil, and anise oil. (A64,6:24-40). FIG. 4 plots the

temperature at which an endothermic peak (*i.e.*, melting point) was observed for CoQ₁₀ crystals for each volatile essential oil as a function of the ratio of CoQ₁₀:essential oil. (A64,6:27-34). A copy of FIG. 4 (A52) is reproduced below with text boxes and highlighting of the lemon oil plot added.

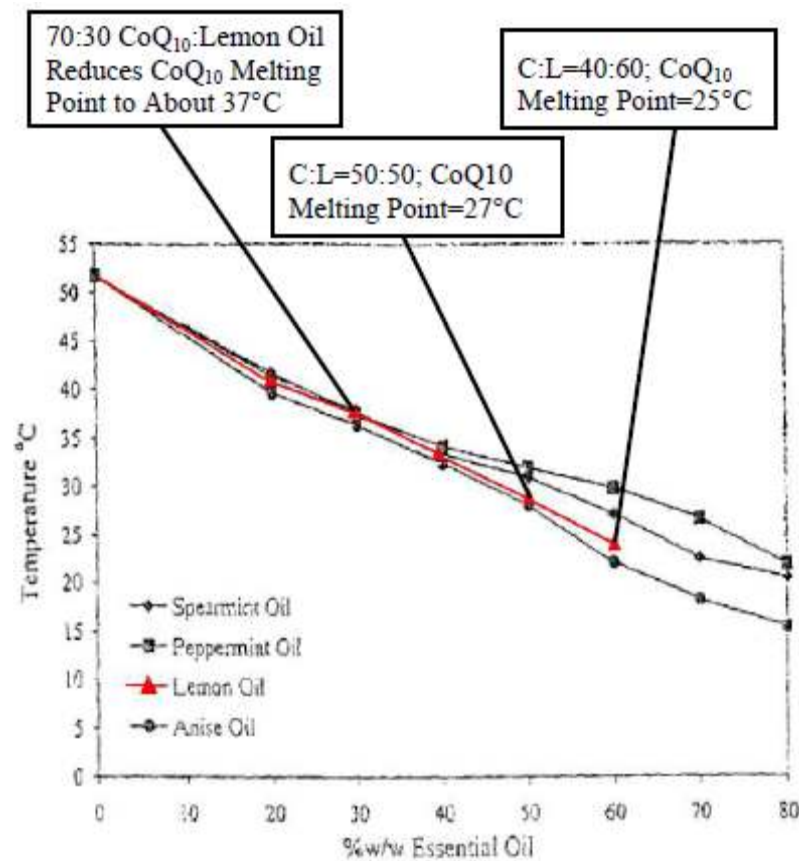


FIG. 4

Dr. Williams testified that d-limonene is lemon oil, and that in the context of the melting point data of FIG. 4, “d-limonene behaves exactly like lemon oil.” (A387, ¶36; A1210-11, 182:5-183:10). As shown by the second lemon oil data point in FIG. 4 above, a 30:70 ratio of lemon oil (or d-limonene oil) to CoQ₁₀

reduces the melting point of CoQ₁₀ to about 37°C. Increasing the amount of lemon oil (or d-limonene oil) to CoQ₁₀ beyond a 30:70 ratio progressively decreases the melting point of CoQ₁₀ below 37°C, as shown by the following table of data points from FIG. 4:

<u>Ratio of CoQ₁₀ to Lemon Oil (C:L)</u>	<u>Melting Point of CoQ₁₀ (°C)</u>
C:L=70:30	37°C
C:L=60:40	33°C
C:L=50:50	27°C
C:L=40:60	25°C

In sum, the FIG. 4 melting point data demonstrates that increasing the amount of lemon oil (or d-limonene oil) so that it is equal to the amount of CoQ₁₀ reduces the melting point of CoQ₁₀ to about 27°C, and increasing the amount of lemon oil (or d-limonene oil) to 1-1/2 times the amount of CoQ₁₀ (*i.e.*, a 60:40 ratio) reduces the melting point of CoQ₁₀ to about 25°C. (A52). 25°C is within the room temperature range, and both 27°C and 25°C are well below body temperature (37°C). (A396, ¶¶69&n.59; A381, ¶¶20).

VI. THE CLAIMED INVENTION

The claims of the '786 patent are directed to an orally administered dietary supplement comprising:

“a) ubiquinone; and

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b) a sufficient amount of a volatile essential oil to solubilize the ubiquinone, and wherein said volatile essential oil is present in a sufficient amount to reduce the melting point of ubiquinone to 37°C, or below, and thereby solubilize the ubiquinone comprised in the orally administered dietary supplement at or below body temperature.” (A71,19:28-36).

VII. THE ACCUSED SUPPLEMENTS USE MORE THAN ENOUGH D-LIMONENE OIL TO REDUCE THE MELTING POINT OF COQ₁₀ TO 37°C OR BELOW

The Accused Supplements include CoQ₁₀ or ubiquinone and d-limonene. (A806-30; A865-74; A891-932). Some of the Accused Supplements include ubiquinol which is the reduced form of CoQ₁₀ or ubiquinone. (A831-34; A875-90).

D-limonene is a volatile essential oil. (A385-86,¶31; A1098,¶29). Williams opined that (i) lemon oil is 90% d-limonene, (ii) d-limonene is the major volatile essential oil derived from the rind of lemons, and (iii) d-limonene literally is lemon oil, or is insubstantially different from lemon oil. (A385-86,¶31, A387-388,¶¶36-37, A392-93,¶53). [REDACTED]

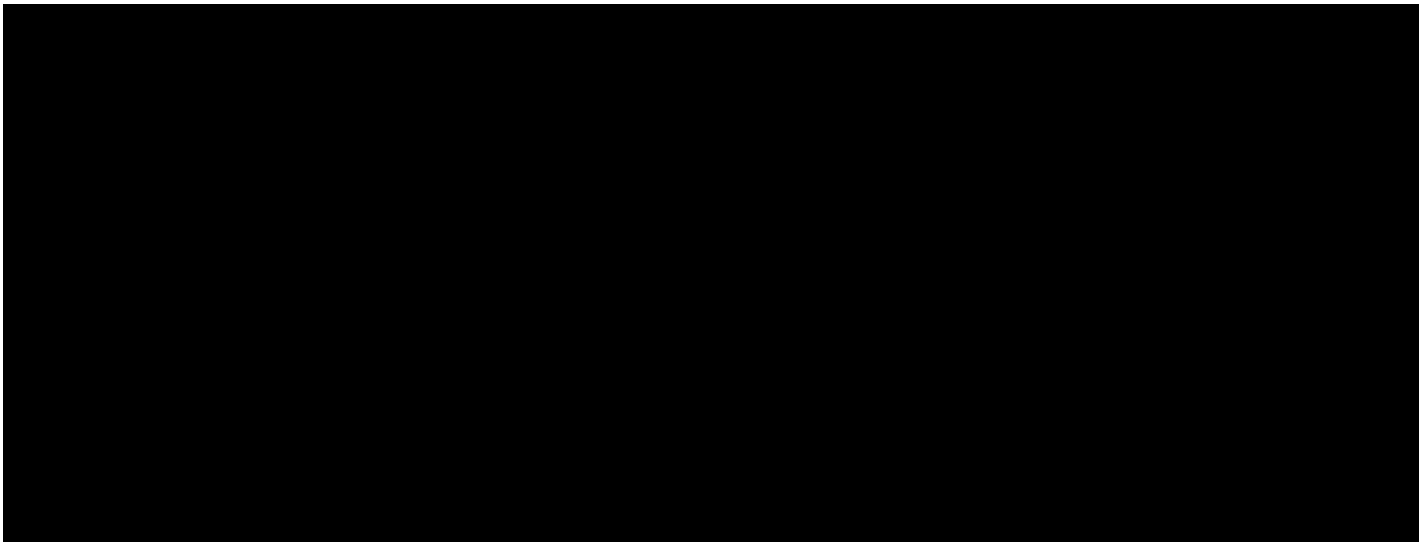
(A868).

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A. The Accused Supplements Include [REDACTED] the Amount of D-Limonene Oil to CoQ₁₀, Which Is More Than Enough D-Limonene Oil to Reduce the Melting Point of CoQ₁₀ to 37°C or Below

The CoQ₁₀:d-limonene oil ratios of the Accused Supplements are shown by Soft Gel's Formulation Cost sheets, which describe the ingredients, the relative weights of the ingredients, and the costs of the ingredients used to formulate the Accused Supplements. (A806-34). The Cost Formulation sheets use intuitive prefixes to identify the respective ingredients, [REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED] (e.g., A831-34).

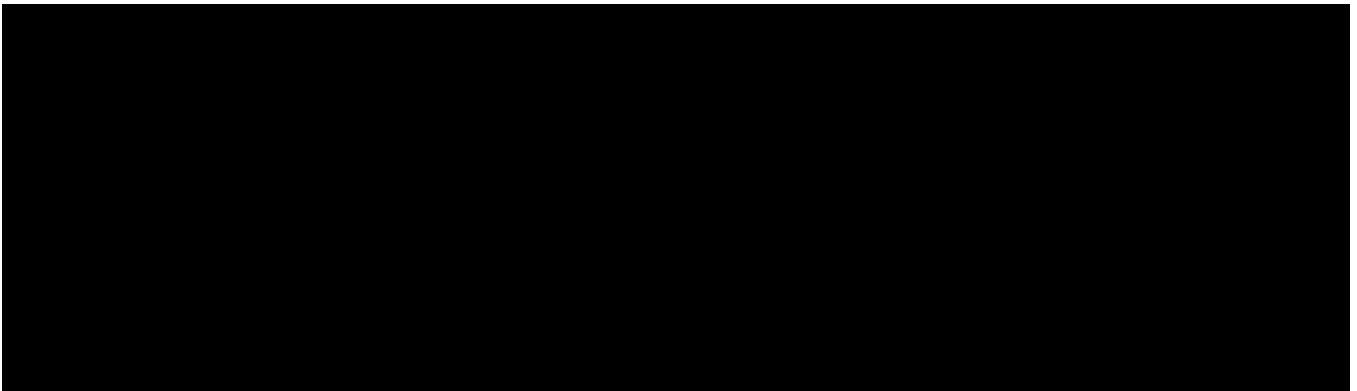
The following image shows the pertinent portion of an exemplary Cost Formulation Sheet (A806):



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The amount by weight of CoQ₁₀ (“CO-00016”) is [REDACTED], the amount by weight of d-limonene oil (“LI-00454”) is [REDACTED], and therefore the CoQ₁₀:d-limonene oil ratio is [REDACTED]³

The same information is set forth in Soft Gel’s “Master Formula” sheets. (A865-932). Like the Cost Formulation Sheets, the Master Formula sheets describe the ingredients, the relative weights of the ingredients, and the costs of the ingredients used to formulate the Accused Supplements. The following image shows the descriptive portion of the Master Formula sheet for the Accused Supplement formulation corresponding to the Cost Formulation sheet image above. (A865).



The Master Formula sheet uses the same intuitive prefixes and further describes these ingredients as [REDACTED]

[REDACTED] The relative amounts of the ingredients and, therefore, the CoQ₁₀:d-

³ These weights are converted to a CoQ₁₀:d-limonene weight ratio as follows:
 CoQ₁₀ = [REDACTED] x 100% = [REDACTED]; d-limonene = [REDACTED]
 [REDACTED] 100% = [REDACTED]; therefore, the ratio is [REDACTED]

limonene ratio is the same as in the corresponding Cost Formulation sheet, *i.e.*,

[REDACTED].

The other Cost Formulation and Master Formula sheets identify the ratios of CoQ₁₀:d-limonene for all Accused Supplements as follows:

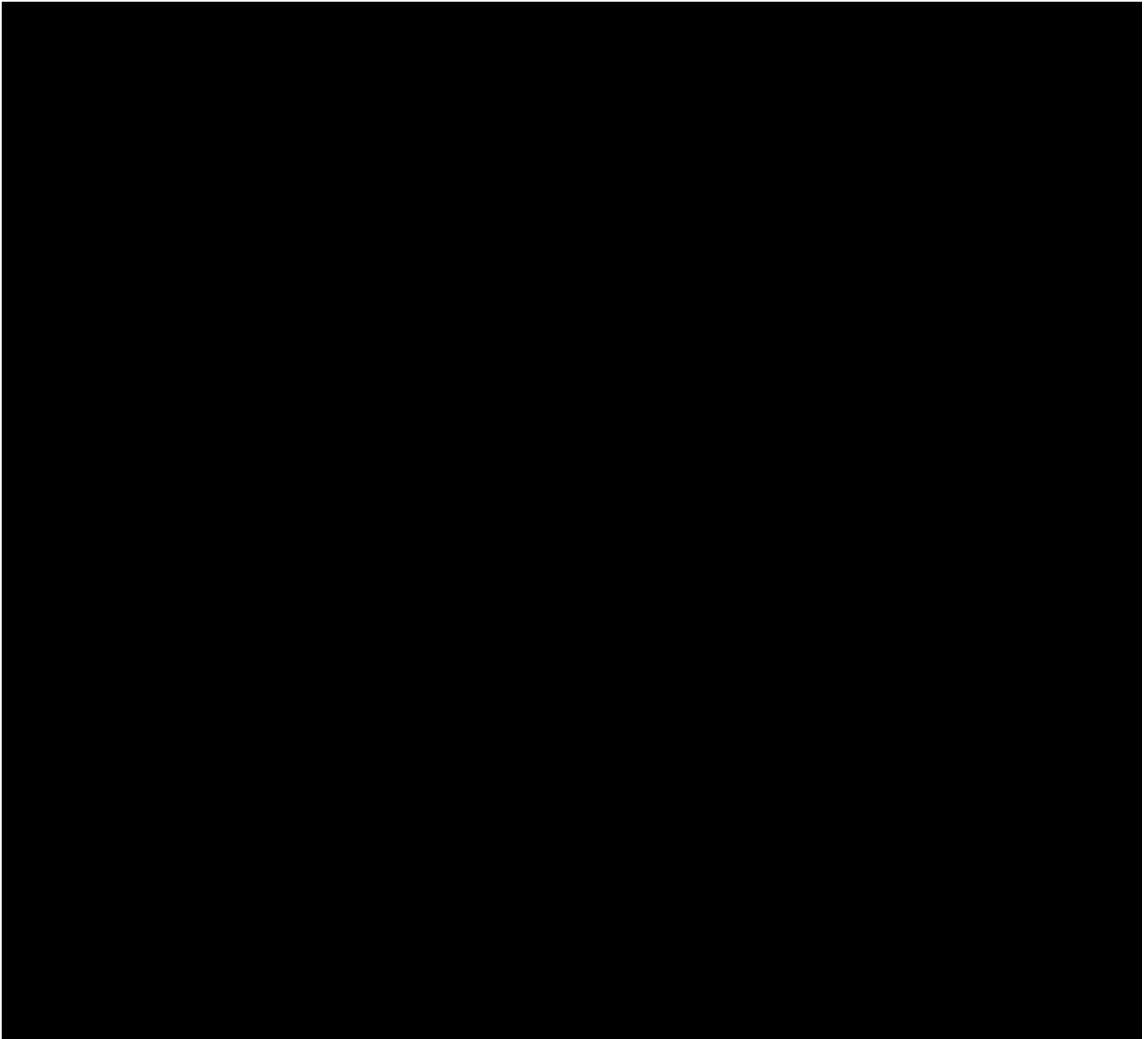


Table 1

In sum, most Accused Supplements include [REDACTED] the amount of d-limonene oil to CoQ₁₀; the two “ubiquinol” formulations include [REDACTED] the amount of d-limonene oil to ubiquinol; and one formulation (TK-9029M) includes [REDACTED] the amount of d-limonene oil to CoQ₁₀.

As demonstrated by the melting point data in FIG. 4, *supra*, p. 11-12, less than one-half the amount of lemon oil (or d-limonene oil) to CoQ₁₀ (*i.e.*, a 30:70 ratio) reduces the melting point of CoQ₁₀ to about 37°C; equal amounts of lemon oil and CoQ₁₀ reduce the melting point to about 27°C; and 1-1/2 times the amount of lemon oil to CoQ₁₀ reduces the melting point to about 25°C. The Accused Supplements include [REDACTED] the amount of d-limonene oil to CoQ₁₀, which, based on the melting point data of FIG. 4, is [REDACTED] more d-limonene oil than required to reduce the melting point to [REDACTED]. Accordingly, the Accused Supplements include enough d-limonene oil to reduce the melting point to [REDACTED] below body temperature. (A383, ¶26; A1210-11,182:5-183:21; A1212,187:6-21).

B. The Accused Supplements Are Manufactured by [REDACTED], Which Melts the CoQ₁₀

Each Accused Supplement is manufactured by [REDACTED]

[REDACTED]. Soft Gel’s Master Formula sheets (A865-932) include “blending

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instructions” setting forth the order and manner in which the ingredients identified in the respective “Master Formula” are blended. Each set of “blending instructions” [REDACTED]

[REDACTED]

[REDACTED] An exemplary set of such blending instructions, with pertinent portions highlighted, is copied below (A865):

[REDACTED]

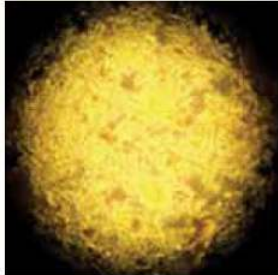
[illegible]

[REDACTED], the CoQ₁₀ remains melted. Soft Gel conducted microscopic analyses on the Accused Supplement formulations, and in each case, the CoQ₁₀ was liquid and crystal free at room temperature. Soft Gel's analysis could not detect under microscopic inspection even submicron particulate matter. (A743, A755).

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Introducing **CoQsol-CF®** from **Soft Gel Technologies**, a completely soluble, liquid, crystal-free solution of CoQ₁₀ clinically proven to provide superior bioavailability of this key nutrient.

Solubility



CoQ₁₀ Paste

Bioavailability

CoQsol-CF® is a unique, patent-pending formulation of CoQ₁₀, d-Limonene, and natural tocopherols (vitamin E). Upon microscopic examination at 200x, a paste of CoQ₁₀ powder and soybean oil exhibits a crystalline structure, while CoQsol-CF® is completely devoid of crystals because the CoQ₁₀ has been solubilized.

Absorption



CoQsol-CF®

In the soybean oil formulation on the left, the melting point of the CoQ₁₀ is above room temperature, and therefore the CoQ₁₀ exhibits a visible crystalline structure. In the Accused Supplement image on the right, there is a sufficient amount of d-limonene oil to depress the CoQ₁₀ melting point so that it is “liquid”, “crystal-free” and solubilized at room temperature. (A382, ¶26; A527-28, 163:4-164:22).

Soft Gel summarized its microscopic analyses of the Accused Supplements demonstrating that the CoQ₁₀ remains melted at room temperature, in pertinent part as follows (A743):

- **High-intensity microscope light.** A sample of CoQsol-CF® was placed into a clear glass vial. When a high-intensity microscope light was directed through the container, no scattered light was observed, due to near sub-micron particulate matter.
- **100x dark field microscope.** A sample of CoQsol-CF® was placed under a 100x dark field microscope, which is able to detect the presence of very small particles. There was no evidence of large crystalline — nor of near-micron sized — particulate matter.
- **Instrumental analysis.** A sample of CoQsol-CF® was placed into several instruments able to detect particulate material down to at least 1 part per million. No submicron particulate was detected.

Accordingly, the CoQ₁₀ of the Accused Supplements remains melted at room temperature despite the addition of other ingredients to [REDACTED] [REDACTED]. (A382,¶24; A1206-07,162:21-163:18; A1212,187:6-15). This is consistent with the teachings of the '786 patent, where it is assumed that other ingredients will be added: "Four essential oils ... were evaluated for their eutectic efficacy in the presence of other formulation excipients." (A65,7:6-9). Table 2 shows that lemon oil was best able to melt and solubilize the CoQ₁₀ at 37°C when an excipient was added to the binary mixture. (A65,7:4-34). Lemon oil melted and solubilized the CoQ₁₀ at 37°C even when the concentration of the excipient was 60% by weight of the total. (A65,7:40-44) ("When 60% w/w of cremophor EL [*i.e.*, the excipient] was added, preparations made with 50 and 60% w/w lemon oil to CoQ₁₀ melted within 5.3 and 1.8 min, respectively."). The Accused Supplements typically include [REDACTED] by weight of other ingredients added to [REDACTED]. (A806-34; A865-932).

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SUMMARY OF ARGUMENT

1. There are significant facts in the summary judgment record that were introduced prior to the stricken Williams and Nazzal Declarations showing that the Accused Supplements include a sufficient amount of d-limonene oil to reduce the melting point of ubiquinone to 37°C or below, and that preclude summary judgment of non-infringement. Williams establishes that d-limonene is lemon oil, and that in the context of the melting point data of FIG. 4, “d-limonene behaves exactly like lemon oil.” FIG. 4 sets forth detailed melting point data showing that a 30:70 weight ratio of lemon oil (or d-limonene oil) to ubiquinone reduces the melting point of ubiquinone to about 37°C, and that increasing the amount of lemon oil to ubiquinone reduces the melting point even further. Accordingly, equal amounts of lemon oil and ubiquinone reduce the melting point to about 27°C, and 1-1/2 times the amount of lemon oil as compared to ubiquinone reduces the melting point to about 25°C. The Accused Supplements include [REDACTED] the amount of d-limonene oil to ubiquinone, which, based on the melting point data of FIG. 4, is [REDACTED] more d-limonene oil than required to reduce the melting point to [REDACTED]. Accordingly, the facts show that the Accused Supplements contain more than enough d-limonene oil to reduce the melting point of ubiquinone to 37°C or below, as required by the claims.

Soft Gel's advertising confirms that each Accused Supplement formulation is "a completely soluble, liquid, crystal-free solution of CoQ₁₀...." Soft Gel's advertising further explains how the Accused Supplements were microscopically analyzed with "instruments able to detect particulate material down to at least 1 part per million," and that these instruments could not detect in the liquid CoQ₁₀ even "submicron particulate." Accordingly, the facts show that the ubiquinone is melted in the binary mixtures, and that it remains melted at or below 37°C

3. The District Court abused its discretion by excluding the May 4 and May 25 Declarations as “new opinions.” In his expert report on infringement and in his

deposition testimony, Williams opined that the Accused Supplements infringe the '786 patent based upon the melting point data for CoQ₁₀ and lemon oil in FIG. 4, the evidence that lemon oil is at least 90% d-limonene, the relative ratios of CoQ₁₀ and d-limonene in the Accused Supplements, and Soft Gel's advertisements. The May 4 Declaration sets forth Williams' infringement opinion together with tables and figures illustrating and presenting his opinion. The May 25 Declaration provided Williams' rebuttal to Soft Gel's criticism of his opinion. Williams is allowed to provide testimony that explains his opinions together with exhibits that illustrate those opinions. Further, he is allowed to rebut criticism. The District Court erred by concluding otherwise.

4. The District Court also abused its discretion by excluding, as undisclosed expert opinion, the Nazzal Declaration. The Nazzal Declaration provides factual testimony from a co-inventor regarding the tests that he performed as described in the '786 patent, his personal observations of the results of those tests, and his description of how the invention described in the patent works. This factual testimony from an inventor is routinely admitted into evidence in patent cases, and the District Court erred in excluding his declaration.

ARGUMENT

I. INFRINGEMENT

A. Legal Principles and Standard of Review

This Court reviews summary judgment decisions under regional circuit law. *Frolov v. Wilson Sporting Goods Co.*, 710 F.3d 1303, 1308 (Fed. Cir. 2013). The Ninth Circuit reviews the grant of summary judgment *de novo*. *Goodman v. Staples The Office Superstore, LLC*, 644 F.3d 817, 822 (9th Cir. 2011).

Determining whether a device infringes a patent claim is a two-step process. First, the court must construe the claims at issue. Second, the Accused Supplements must be compared to the properly construed claim to determine whether each and every limitation of the claim is met, either literally or by equivalents. *Cook Biotech Inc. v. Acell, Inc.*, 460 F.3d 1365, 1372 (Fed. Cir. 2006). Literal infringement requires that “every limitation recited in the claim is found in the accused device.” *Engel Indus., Inc. v. Lockformer Co.*, 96 F.3d 1398, 1405 (Fed. Cir. 1996).

Under the *de novo* standard, this Court “reviews without deference a district court’s grant of summary judgment and draws all reasonable factual inferences in favor of the non-movant.” *Toro Co. v. White Consol. Indus., Inc.*, 266 F.3d 1367, 1369 (Fed. Cir. 2001); *Ethicon Endo Surgery, Inc. v. U.S. Surgical Corp.*, 149 F.3d 1309, 1315 (Fed. Cir. 1998). Summary judgment is proper only if there are no genuine issues of material fact and the movant is entitled to judgment as a matter

of law. *See* Fed. R. Civ. P. 56(a); *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 255 (1986).

Infringement is a question of fact. *Crown Packaging Tech., Inc. v. Rexam Beverage Can Co.*, 559 F.3d 1308, 1312 (Fed. Cir. 2009). In the summary judgment setting, the proper inquiry is whether, drawing all justifiable inferences in favor of the non-moving party, the evidence is such that a reasonable jury could return a verdict for the non-movant. *See id.*; *In re Gabapentin Patent Litig.*, 503 F.3d 1254, 1259 (Fed. Cir. 2007). The District Court cannot “invade[] the province of the finder of fact...in deciding the infringement question.” *Dorel Juvenile Grp., Inc. v. Graco Children’s Prods., Inc.*, 429 F.3d 1043, 1047 (Fed. Cir. 2003) (reversing summary judgment of noninfringement because the infringement inquiry included “a question of fact that cannot be determined on summary judgment”). Where the evidence “points in both directions....[i]t is the job of the fact-finder—not the court at summary judgment—to weigh that evidence and render a decision.” *Frolow*, 710 F.3d at 1311 (citation omitted).

B. The Asserted Claims and Limitations in Dispute

Jarrow asserts infringement of claims 1-6, 8-10, 12 and 13. At summary judgment, Soft Gel and NOW disputed (i) the melting point reduction limitation, *i.e.*, whether the Accused Supplements include a sufficient amount of volatile essential oil to reduce the melting point of ubiquinone to 37°C or below, and (ii)

whether the “ubiquinone” limitation covers those Accused Supplements that contain “ubiquinol”. (A999-1004). Soft Gel and NOW also argued that the term “eutectic” in the preambles of claims 1 and 10 is a limitation, and disputed whether the Accused Supplements would infringe this term if it were a limitation. (A997-99, A1002).

C. The District Court’s Claim Construction and Summary Judgment Rulings

The District Court construed “‘melting point’ to mean ‘the temperature at which a chemical agent has a transition from solid to liquid due to the application of heat’”, and “‘reduc[tion of] the melting point’ to require ‘a change or modification of the physical properties of ubiquinone; *i.e.*, depression of its melting point,” and not merely dissolution.”⁴ (A21).

The District Court determined that the term “eutectic-based delivery system” in the preambles of claims 1 and 10 is not a limitation. (A13-16). However, the District Court found that the admissible evidence “provides no basis from which a jury could conclude that the CoQ10 in the Accused Supplements is liquid at or below 37[°]C due to a change in its physical properties, *i.e.*, a reduction in its

⁴ In issuing this construction, the District Court adopted Soft Gel’s clarification at the Markman hearing “that the ‘application of heat’ was not necessarily a separate step to be performed in all cases. Rather, ‘application of heat’ requires only the presence of a sufficient temperature to work the physical change. Therefore, where a substance melts below room temperature, ... the ambient temperature itself supplies the requisite ‘application of heat.’” (A17, n.3).

melting point”, and therefore granted summary judgment of non-infringement for this reason. (A30). The District Court declined to construe the term “ubiquinone” on grounds that it was not essential to the infringement analysis. (A21,n.5).

D. The Evidence Demonstrates That the Accused Supplements Include a Sufficient Amount of Volatile Essential Oil to Reduce the Melting Point of Ubiquinone to 37°C or Below

The District Court erred in granting summary judgment of non-infringement because there is substantial evidence in the summary judgment record that the Accused Supplements infringe the melting point reduction limitation. Further, this evidence was in the pre-May 2, 2012 record, and therefore was not stricken with the Nazzal and Williams Declarations. Therefore, even if this Court were to affirm the District Court's decision striking the Nazzal and Williams Declarations, which Jarroo submits would be incorrect, *see infra*, pp. 40-63, there are nevertheless disputed issues of fact that preclude summary judgment of non-infringement.

1. The Accused Supplements Infringe the “Ubiquinone” and “Volatile Essential Oil” Limitations

There is no dispute that the d-limonene oil used in the Accused Supplements literally infringes the “volatile essential oil” limitation. (A1098, ¶29; A752-53). Nor is there any dispute that the Accused Supplements that contain “ubiquinone” literally infringe the “ubiquinone” limitation. (A1096, ¶25). The only dispute with respect to the “ubiquinone” limitation is whether the Accused Supplements containing the reduced form of ubiquinone or CoQ₁₀, *i.e.*, ubiquinol, infringe this

limitation. (A1096-1098, ¶¶26-27). The Accused Supplement formulations that use ubiquinol are identified as formula nos. [REDACTED] in Table 1 above. *Supra*, p. 16. The District Court did not address this issue and, in any event, as set forth below, *infra*, pp. 39-40, there are disputed issues of fact that preclude summary judgment on this issue.

2. The Accused Supplements Include More Than Enough D-Limonene Oil to Reduce the Melting Point of Ubiquinone to 37°C or Below

Williams testified that d-limonene is lemon oil, and that in the context of the melting point data of FIG. 4, “d-limonene behaves exactly like lemon oil.” (A1210-11,182:5-183:10; *see also* A387-88, ¶¶36-37). Williams compared the relative amounts by weight of ubiquinone and d-limonene oil in the Accused Supplements to the melting point data of FIG. 4, and concluded, based on the melting point data, that the Accused Supplements include a sufficient amount of d-limonene oil to reduce the melting point of ubiquinone to 37°C or below. (A1210-11,182:5-183:21; A383, ¶26).

Most Accused Supplements include [REDACTED] the amount of d-limonene oil to ubiquinone, the two “ubiquinol” formulations include [REDACTED] the amount of d-limonene oil to ubiquinol, and one formulation (TK-9029M) includes [REDACTED] the amount of d-limonene oil to ubiquinone. *Supra*, pp. 17-18.

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As summarized above, *supra*, pp. 11-12, the melting point data in FIG. 4 demonstrates that less than one-half the amount of lemon oil (or d-limonene oil) as compared to CoQ₁₀ (*i.e.*, a 30:70 ratio) reduces the melting point of CoQ₁₀ to about 37°C; equal amounts of lemon oil and CoQ₁₀ reduce the melting point to about 27°C; and 1-1/2 times the amount of lemon oil to CoQ₁₀ reduces the melting point to about 25°C. The melting point data of FIG. 4 does not indicate the temperature at which the ubiquinone merely dissolves. Rather, each data point in FIG. 4 is the temperature at which an endothermic peak (*i.e.*, melting point) was observed for CoQ₁₀ crystals for each volatile essential oil as a function of the ratio of CoQ₁₀:essential oil. (A63,3:35-37;6:33-40). Thus, the data points in FIG. 4 indicate the temperatures at which the ubiquinone undergoes a change in physical properties, *i.e.*, a transition from a solid to a liquid, due to the application of heat. (*Id.*). Moreover, Soft Gel's expert, Dr. Dash, admits that he has no basis to challenge the accuracy of the melting point data of FIG. 4. (A782,23:9-20; A783,24:7-13; A784,25:16-24). The Accused Supplements include [REDACTED] the amount of d-limonene oil as compared to CoQ₁₀, which, based on the melting point data of FIG. 4, is [REDACTED] d-limonene oil than required to reduce the melting point of CoQ₁₀ to [REDACTED]. Accordingly, the Accused Supplements necessarily contain a sufficient amount of d-limonene oil to reduce the melting point of ubiquinone to 37°C or below.

Williams' conclusion that the Accused Supplements infringe the melting point reduction limitation was reinforced by the fact that Soft Gel advertised the Accused Supplements as "completely soluble, liquid, crystal-free" solutions of CoQ₁₀ at room temperature, which is significantly below the 37°C limitation recited in the claims. (A737-59). These advertisements state that the Accused Supplements were subjected to microscopic analyses where the instruments were able to detect particulate material down to at least 1 part per million, and that such testing could not detect even submicron particulate in the liquid CoQ₁₀. (A742-43, A755). These admissions by Soft Gel that the CoQ₁₀ is "liquid" and "crystal-free" at room temperature, coupled with the melting point data of FIG. 4 demonstrating that the Accused Supplements have [REDACTED] d-limonene oil than required to reduce the melting point of ubiquinone to 37°C or below, show that the Accused Supplements infringe the melting point reduction limitation.

Accordingly, there are significant facts in the summary judgment record that were introduced prior to the stricken Williams and Nazzal Declarations showing that the Accused Supplements infringe the melting point reduction limitation, and that preclude summary judgment of non-infringement.

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3. Soft Gel's Criticism of Williams' Infringement Analysis on Grounds That the Accused Supplements Include "Other Ingredients" Is Without Merit

Soft Gel criticizes Williams for comparing the ubiquinone:d-limonene ratios in the Accused Supplements to the melting point data in FIG. 4 on grounds that FIG. 4 pertains to binary mixtures only, that the Accused Supplements are not binary mixtures, and that the other ingredients could affect the melting point reduction. (A1003-04). However, each Accused Supplement is manufactured by

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]. *Supra*, pp. 17-18. [REDACTED]

[REDACTED],

based on the melting point data of FIG. 4, is [REDACTED] d-limonene oil than required to reduce the melting point of CoQ₁₀ to [REDACTED]. Accordingly, the melting point of ubiquinone in each mixture is [REDACTED]

[REDACTED]

[REDACTED]

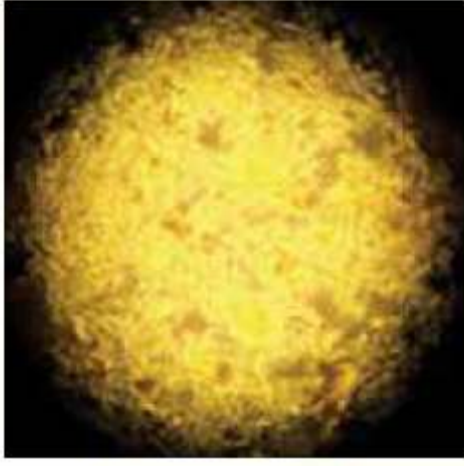

[REDACTED]


[REDACTED]

[REDACTED] (*E.g.*, A865). The

remaining ingredients do not cause the melted ubiquinone to transition from a liquid to a solid. Rather, Soft Gel's advertisements repeatedly state that the Accused Supplements are "crystal free." (A382, ¶24). One of the advertisements reviewed by Williams states that the Accused Supplement formulation was analyzed with "several instruments able to detect particulate material down to at least 1 part per million," and that not even "submicron particulate was detected" in the liquid CoQ₁₀. (A743). These statements by Soft Gel further demonstrate that the ubiquinone remains melted at room temperature (about 20-25°C). (A1206-07,162:21-163:18; A1212,187:6-15). The following images at 200x magnification at room temperature (significantly below 37°C) illustrate the point. On the right, the ubiquinone in the Accused Supplements remains liquid and crystal free. In stark contrast, on the left, CoQ₁₀ mixed with soybean oil is not melted but rather exhibits a solid or crystalline structure (A742):

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 <p>CoQ₁₀ Paste</p>	 <p>CoQsol-CF®</p>
<p><u>200X Magnification of CoQ₁₀ in Soybean Oil – CoQ₁₀ Not Melted</u></p>	<p><u>200x Magnification of Accused Supplement – CoQ₁₀ Melted</u></p>

 does not cause the ubiquinone to transition from a liquid to a solid, but rather the ubiquinone remains melted at room temperature, which is significantly below 37°C, as Williams opined. (A383,¶24; A1212,187:6-21).

Soft Gel may quibble with Williams' analysis, but its criticisms only underscore the existence of a genuine issue of fact for trial. *See Caterpillar Inc. v. Deere & Co.*, 224 F.3d 1374, 1380 (Fed. Cir. 2000) (reversing grant of summary judgment of non-infringement upon concluding "[t]he expert testimony and evidence of known interchangeability were more than sufficient to create a genuine issue of material fact..."); *see also Brilliant Instruments, Inc. v. GuideTech, LLC*, 707 F.3d 1342, 1348 (Fed. Cir. 2013) (reversing grant of summary judgment of

non-infringement and identifying expert testimony as creating a genuine issue of material fact). “[A]s a general rule, the factual basis of an expert opinion goes to the credibility... not the admissibility.” *Neb. Plastics, Inc. v. Holland Colors Americas, Inc.*, 408 F.3d 410, 416 (8th Cir. 2005).

It is only appropriate to exclude expert testimony where it “is so fundamentally unsupported that it can offer no assistance to the jury[.]” *Id.* (excluding damages expert’s testimony based on assumption that 100% of products would be subject to warranty claims when, in fact, only 3.5% were subject to such claims). As the Ninth Circuit has stated, “given that the [trial] judge is ‘a gatekeeper, not a fact finder’...the gate [cannot] be closed to [a] relevant opinion offered with sufficient foundation by one qualified to give it.” *Primiano v. Cook*, 598 F.3d 558, 568 (9th Cir. 2010) (reversing exclusion of expert testimony and reversing grant of summary judgment).

Here, Williams’ opinions establish infringement. Thus, at the very least, there are disputed issues of fact as to whether there is a sufficient amount of d-limonene oil in the Accused Supplements to reduce the melting point of ubiquinone to 37°C or below. The District Court impermissibly weighed the evidence and discredited it. Contrary to the approach taken by the District Court, the “court must assume that the evidence presented by the non-movant is credible and draw all justifiable inferences therefrom in [Jarrow]’s favor.” *See Loral*

Fairchild Corp. v. Matsushita Elec. Indus. Co., Ltd., 266 F.3d 1358, 1361 (Fed. Cir. 2001).

4. Soft Gel's Arguments Do Not Erase the Disputed Issues of Fact That Preclude Summary Judgment

Soft Gel argues that the melting point data of FIG. 4 cannot prove infringement because the “patent, file history and Dr. Williams all agree ... that eutectics and melting point reduction cannot be predicted, but rather must be empirically determined with chemical assays that take into account all the ingredients in the mixture.” (A1003 (emphasis original)). This argument improperly conflates infringement and validity. There is no dispute that at the time of the ‘786 invention it could not be predicted whether combinations of CoQ₁₀ and essential oils would reduce the melting point of CoQ₁₀ to 37°C or below. *See Amgen Inc. v. F. Hoffmann-La Roche Ltd.*, 580 F.3d 1340, 1362-63 (Fed. Cir. 2009) (obviousness measured at time invention made). However, the ‘786 patent teaches how CoQ₁₀ can be combined with different essential oils, and how the proportions of CoQ₁₀ to essential oils can be adjusted to reduce the melting point of CoQ₁₀ to a desired level. (A64,6:27-34; A65,7:19-34). Further, the ‘786 patent teaches that additional ingredients can be added to binary mixtures of CoQ₁₀ and essential oil while nevertheless maintaining a reduced melting point of the CoQ₁₀. (A64-65,6:42-7:60). The ‘786 patent rendered predictable what was previously unpredictable absent its teachings. *See Noelle v. Lederman*, 355 F.3d 1343, 1351-

52 (Fed. Cir. 2004) (expectation of success cannot come from applicant's disclosure).

Soft Gel contends that co-inventor Dr. Khan "published a journal article concluding that d-limonene did not reduce the melting point of ubiquinone." (A1004). This is incorrect. The article reports on the melting point of one binary mixture of 90% CoQ₁₀ and only 10% d-limonene. (A1024). This mixture was not tested in FIG. 4 above, and included much less than the lowest amount tested (which was 20% lemon oil or 18% d-limonene). (A52; A468-69, ¶¶33-34). The article does not controvert the test data of FIG. 4 showing that increasing the percentage of lemon oil (or d-limonene oil) beyond 30% progressively decreases the melting point of the CoQ₁₀ below 37°C. (A466-67, ¶30).

At pages 15-16 of its decision, the District Court incorrectly found that Williams had based his opinion on a definition of "melting point" as synonymous with "dissolving". (A22-23). To the contrary, Williams' deposition testimony is clear that he applied the term in exactly the way it was construed by the District Court. When asked at his deposition what he meant by the term "melting point" in his report, Williams stated that "it's a temperature at which a - an agent, a chemical agent, is going to have a solid-to-liquid transition. That's called the melting point." (A493-94, 41:15-42:2). Williams also testified that, generally, melting point is discussed "in the context of an application of heat or it being at a certain

temperature.” (A494-95,42:25-43:1). This is consistent with the District Court’s construction of the term.

As stated in his report and at his deposition, Williams compared the relative ratios of CoQ₁₀ and d-limonene in the Accused Supplements to the melting point data for lemon oil (*i.e.*, d-limonene oil) in FIG. 4, and concluded that the melting point of the CoQ₁₀ was reduced to less than 37°C as recited in the claims. (A383,¶26; A1210-11,182:5-183:10). The District Court dismissed Williams’ infringement analysis, stating that his opinion “was still rooted in the faulty premise that the melting point reduction limitation required only that the ubiquinone be in a liquid state at or below 37C.” (A24-25). However, throughout his expert report, Williams states that the reduction in the melting point of CoQ₁₀ is the process by which the CoQ₁₀ is solubilized in the essential oil. (A386,¶32; A462,¶20). When sufficient essential oil is present, the CoQ₁₀ melts and forms an “oily phase” in the essential oil at or below body temperature. (A64,6:36-40). This is borne out by the melting point data in FIG. 4 that was relied upon by Williams. Once the melting point reduction to 37°C or below is achieved, the CoQ₁₀ is necessarily a liquid and thereby solubilized, and the claim limitation is met. When Williams’ expert report and deposition testimony are fully considered, it is clear that he applied the correct definition of “melting point” and determined that the Accused Supplements infringe the melting point reduction limitation based

upon the melting point data of FIG. 4. Williams cited to the Soft Gel advertisements as also supporting his opinion that the melting point of the CoQ₁₀ was sufficiently reduced to solubilize the CoQ₁₀ at 37°C because the Accused Supplements have no crystal CoQ₁₀ and are “100% solubilized” at room temperature. (A382, ¶24; A1206-07, 162:21-163:18).

In sum, there is substantial evidence that the Accused Supplements include a sufficient amount of d-limonene oil to reduce the melting point of ubiquinone to 37°C or below. This evidence must be viewed in the light most favorable to Jarrow, with all reasonable inferences drawn in its favor. When so viewed, there is, at the very least, a disputed issue of fact that precludes summary judgment of non-infringement.

5. The District Court Did Not Address Whether Accused Supplements Containing “Ubiquinol” Infringe the “Ubiquinone” Limitation, and Therefore This Issue Must Be Remanded

Soft Gel admits that, in the context of the patent, “ubiquinone” means “CoQ₁₀” (A1069, ¶2; A1093, ¶16), and “ubiquinol” is the “the reduced form of CoQ₁₀”. (A1096, ¶26; A768). Williams opined that “ubiquinone” and “ubiquinol” “are simply redox states of the same compound”, and therefore ubiquinol literally meets the ubiquinone limitation. Alternatively, Williams provided a detailed analysis as to why ubiquinol is insubstantially different from ubiquinone, and performs the same function, in the same way, to achieve the same result as

ubiquinone. (A384-385, ¶29-30). Accordingly, at the very least, there are disputed issues of fact as to infringement of this limitation.

Soft Gel argued to the District Court that “CoQ10 is short hand for ubiquinone and Coenzyme Q10, but these terms cannot be construed to cover ubiquinol.” (A1001). Soft Gel’s argument led the District Court to incorrectly characterize this as a claim construction issue rather than an infringement issue. The District Court stated that it declined to reach the claim construction issue as not essential to its non-infringement determination. (A21,n.5). Therefore, even if it is viewed as a claim construction issue, remand to the District Court is required. *See O2 Micro Int’l Ltd. v. Beyond Innovation Tech. Co.*, 521 F.3d 1351, 1362-63 (Fed. Cir. 2008) (remanding case to district court for determination of proper construction of claim in first instance).

II. THE DISTRICT COURT ABUSED ITS DISCRETION BY EXCLUDING IMPORTANT EXPERT AND FACT EVIDENCE

The District Court wrongly struck the May 4 and May 25 Declarations, and the Nazzal Declaration. In so doing, the Court excluded evidence that further established infringement of the ‘786 patent.

A. Standard of Review

This Court reviews a district court's decision to exclude evidence under the law of the regional circuit. *Tokai Corp. v. Easton Enters., Inc.*, 632 F.3d 1358, 1364 (Fed. Cir. 2011). The Ninth Circuit reviews a district court's decision to exclude evidence on summary judgment under an abuse of discretion standard. *Id.*; *Wong v. Regents of Univ. of Cal.*, 410 F.3d 1052, 1060 (9th Cir. 2005). A district court abuses its discretion when it applies an incorrect legal standard, or when it applies the correct legal standard but does so in a manner that is illogical, implausible, or without support in the record. *United States v. Hinkson*, 585 F.3d 1247, 1261-62 (9th Cir. 2009) (en banc); *see also Lambright v. Ryan*, 698 F.3d 808, 817-822 (9th Cir. 2012) (applying *Hinkson* to district court's management of dispute related to discovery and reversing based on abuse of discretion).

B. The District Court Abused Its Discretion by Excluding the Williams Declarations As Untimely Expert Reports

The District Court excluded important expert evidence when it wrongly concluded that the Williams Declarations were "untimely expert report[s]" containing new opinions not previously disclosed. (A26-29). The exclusion of this evidence was harmful to Jarow. *See Obrey v. Johnson*, 400 F.3d 691, 699-701 (9th Cir. 2005) (prejudice from erroneous evidentiary rulings is presumed).

As to the May 4 Declaration, the Court reasoned that the "deeper analysis" of FIG. 4 of the '786 patent constituted a "new opinion." (A28).

As to the May 25 Declaration, the Court reasoned that Williams' analysis of documents cited by Soft Gel's expert in his criticism of Williams' opinion were "new opinions." (A28).

The Court abused its discretion in both instances.

In his expert report on infringement, Williams provided a summary of the technology of the '786 patent, and his opinion that the Accused Supplements infringed the asserted claims. He stated that his opinion was based upon (1) the information contained in the '786 patent, including the melting point data for CoQ₁₀ and lemon oil of FIG. 4 (A379-381, ¶¶18-20; A383, ¶¶26-27), (2) the evidence showing that lemon oil is at least 90% d-limonene (A387-88, ¶¶36-37; A391, ¶49), (3) the relative ratios of CoQ₁₀ and d-limonene disclosed in Soft Gel's formulation documents (A383, ¶26), and (4) Soft Gel's advertisements and associated testing of the Accused Supplements. (A382, ¶24). In addition, Williams provided in his report a detailed claim chart explaining the bases for his infringement opinion. (A1180-86).

Contrary to the conclusions of the District Court, the Williams Declarations do not present new opinions. Rather, they (i) present information and opinions that were already plainly set forth in his expert report, (ii) provide figures and tables illustrating and explaining his previously stated opinions as he would be permitted to do at trial, and (iii) permissibly rebut Soft Gel's criticism of his opinions.

1. The May 4 Declaration Was Fully Supported by Williams' Expert Report and Did Not Contain New Opinions

The purpose of the expert disclosure requirement of Rule 26(a)(2) is “to convey the substance of the expert’s opinion . . . so that the opponent will be ready to rebut, to cross-examine, and to offer a competing expert if necessary.” *Meyer Intellectual Props. Ltd. v. Bodum, Inc.*, 690 F.3d 1354, 1374-75 (Fed. Cir. 2012) (quoting *Walsh v. Chez*, 583 F.3d 900, 994 (7th Cir. 2009)). “The rule contemplates that the expert will supplement, elaborate upon, explain and subject himself to cross-examination upon his report.” *Thompson v. Doane Pet Care Co.*, 470 F.3d 1201, 1203 (6th Cir. 2006).

In support of Jarrow’s motion for summary judgment of infringement, Williams provided the May 4 Declaration. The first twenty-five paragraphs of the May 4 Declaration are taken directly from Williams’ expert report.⁵

At paragraphs 26 and 27 of the May 4 Declaration, Williams converts the ratios of CoQ₁₀ to lemon oil to ratios of CoQ₁₀ to d-limonene based on the percentage of d-limonene in lemon oil. His expert report states that in order to reach his conclusion of infringement, he relied on the information in FIG. 4 showing the relative ratios of CoQ₁₀ to lemon oil, that lemon oil is at least 90% d-limonene, that d-limonene is lemon oil, and, further, he testified that in the context

⁵ Paragraphs 1-25 of the May 4 Declaration are taken from paragraphs 1-15, 17-20, 22, and 29-32 of Williams’ expert report. *Compare* A614-23 to A369-87.

of the melting point data of FIG. 4, “d-limonene behaves exactly like lemon oil,” . (A380-81,¶¶19-20; A383,¶26; A387,¶36; A391,¶49; A1210,182:22-24). Williams’ deposition testimony confirmed and further explained his opinions at paragraphs 24-32 of his expert report. (A1206-07,162:21-163:18; A1210-11,182:5-183:21).

Paragraphs 26 and 27 of the May 4 Declaration contain no “new” opinions. They merely illustrate and elaborate upon the opinion set forth in Williams’ expert report. As to the “deeper analysis” of FIG. 4 referred to by the District Court, Williams simply converted the ratios of CoQ₁₀ to lemon oil to the ratios of CoQ₁₀ to d-limonene at each data point. There was nothing “deep,” technical, or scientific about this step. Williams stated in his expert report and deposition that the melting point reduction was due to d-limonene, and that in the context of the invention, lemon oil is literally d-limonene, and d-limonene behaves exactly like lemon oil. It was simple mathematics to determine the percentage of d-limonene in the lemon oil at each data point of FIG. 4 (*i.e.*, % lemon oil x 90% = % d-limonene). Indeed, the mathematical computation did not expand upon or change Williams’ opinion in any way. *See Thompson*, 470 F.3d at 1203 (expert allowed to elaborate on and explain opinion provided in expert report).

In paragraph 28 of the May 4 Declaration, and in Exhibit 2 to that declaration, Williams summarizes the ratios of CoQ₁₀ to d-limonene in the

Accused Supplements, and states his opinion that, based on the data provided in FIG. 4, the ratios are amply sufficient to reduce the melting point of CoQ₁₀ to less than 37°C. (A625-26, ¶28). In his expert report, Williams reviewed documents provided by Soft Gel showing the formulations for the Accused Supplements. (A383, ¶26). Williams concluded that the relative ratios of CoQ₁₀:d-limonene oil in the Accused Supplements resulted in the claimed melting point reduction by comparing the ratios from the formulation sheets to the ratios in FIG. 4. (*Id.*).

In the May 4 Declaration, Williams reviewed a second set of formulation documents that had been provided by Soft Gel for the Accused Supplements that he had not reviewed at the time of his expert report. (A865-932). Williams applied the same methodology that he applied to the first set of formulation sheets – he determined the ratio of CoQ₁₀:d-limonene oil in the Accused Supplements, and compared that ratio to the data in FIG. 4. Accordingly, there are no new opinions in paragraph 28 of the May 4 Declaration.

In paragraphs 29-32 of the May 4 Declaration, Williams discusses Soft Gel's advertisements, which describe microscopic analyses performed on the Accused Supplements. (A626-27, ¶¶29-32). These advertisements were cited by Williams in his expert report as forming the basis for his opinions. (A382, ¶24). Indeed, Williams pointed to the statements in the advertisements that the products were

“crystal-free.” *Id.* Accordingly, Williams’ quotations from these advertisements are not “new” opinions and should not have been excluded.

Paragraphs 33-43 of the May 4 Declaration merely refer back to the paragraphs discussed above in analyzing infringement of claims 8, 10 and 12, and for the same reasons discussed above, these paragraphs do not include any new opinions.

All of the opinions set forth in the May 4 Declaration are supported in Williams’ expert report and deposition, and he did not change any of his opinions concerning why the Accused Supplements infringe. The analysis of FIG. 4 in the May 4 Declaration was plainly within the scope of the opinions set forth in Williams’ expert report and deposition, and was permitted elaboration and explanation of his opinions. *Thompson*, 470 F.3d at 1203. Accordingly, the May 4 Declaration was not an “expert report” at all. It merely explained his opinions in a way that would have been admissible had he been on the witness stand at trial.

Indeed, if Williams could not explain what was in his report, there would be no reason for him to testify on direct examination at trial. His report would stand for what it says and he would be subjected to cross examination on its contents. But the rules of evidence are not so restrictive at trial, nor are they so at the summary judgment stage. “When testifying at trial ... expert witnesses are allowed to elaborate on the opinions set out in their expert reports; this elaboration

is not improper evidence.” *Lab. Skin Care, Inc. v. Ltd. Brands, Inc.*, C.A. No. 06-601-LPS, 2011 WL 4005444, at *8 (D. Del. Sept. 8, 2011) (citing *Forest Labs., Inc. v. Ivax Pharm., Inc.*, 237 F.R.D. 106, 113 (D. Del. 2006)). (A1546). Just as Williams would be permitted to explain his opinion, defend it, and address criticisms of it in “real time” at trial, he may do the same at summary judgment. He cannot be hamstrung simply because he did not provide a prior report addressing all of the minutiae in every assault that might be made by Soft Gel.

Furthermore, Williams’ discussion of opinions conveyed during his deposition was indisputably appropriate as a matter of law. Fed. R. Civ. P. 26(e) does not require parties to “provide supplemental or corrective information that has been otherwise made known ... during the discovery process, as ... when an expert during a deposition corrects information contained in an earlier report.” Fed. R. Civ. P. 26(e) Advisory Committee note to 1993 amendment. *See Wiggins v. Belk, Inc.*, No. 4:11-cv-88, 2012 WL 135595, at *3 (S.D. Ga. Jan. 17, 2012) (denying motion to exclude expert affidavit because opinions were consistent with report and were disclosed in deposition). (A1549-50).

The District Court made an error of law by strictly limiting Williams to the literal text of his expert report. Furthermore, to the extent that the District Court determined that the May 4 Declaration was inconsistent with Williams' prior report, this determination was illogical, implausible, and without support in the

2. The May 25 Declaration Did Not Include Any New Opinions and Merely Rebutted Criticism from Soft Gel's Expert

In response to this criticism, Williams provided the May 25 Declaration. (A1215-45). In the May 25 Declaration, Williams states that (1) Soft Gel's Master Formula Sheets show that the Accused Supplements are manufactured [REDACTED]

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demonstrate that the additional ingredients do not increase the melting point of the CoQ₁₀ to above 37°C. (A1223-24, ¶¶13-14).

The District Court incorrectly concluded that by referencing the Master Formula Sheets cited by Dash in his criticism of Williams, and by discussing the manufacturing process disclosed in those documents, Williams somehow offered “new opinions.” (A29). But the May 25 Declaration offers no new opinions, it only defends the original opinions against the criticisms leveled by Dash. This was perfectly appropriate and permissible. *McHugh v. Olympia Entm’t, Inc.*, 37 F. App’x 730, 735 (6th Cir. 2002) (“Nothing in Rule 26 precludes an expert from revising or further clarifying opinions, particularly in response to points raised in the presentation of a case.”). (A1560). *See also Volterra Semiconductor Corp. v. Primarion, Inc.*, 796 F. Supp. 2d 1025, 1039-1040 (N.D. Cal. 2011) (denying motion to strike expert declaration because opposing party had been given fair notice of expert’s opinion, recognizing that in the course of litigation, the positions of the parties and their experts necessarily evolve somewhat as each attempts to respond to the arguments of the other).

Williams was not required in his expert report to anticipate and disprove every possible theory or criticism of his opinion that might be advanced by Soft Gel. *See Warner-Lambert Co. v. Teva Pharm. USA, Inc.*, 418 F.3d 1326, 1341 n.15 (Fed. Cir. 2005) (“A claim for patent infringement must be proven by a

preponderance of the evidence, which simply requires proving that infringement was more likely than not to have occurred.”) (citation omitted). Rule 26(a)(2) does not prevent an expert from rebutting criticism of his expert report or opinion at trial. *See Hill v. Reederei F. Laiesz G.M.B.H., Rostock*, 435 F.3d 404, 423 (3d Cir. 2006) (upholding trial court’s admission of expert testimony that “exceeded the scope of [the expert’s] report,” when the testimony was “elicited in rebuttal” to contradictory testimony at trial). Indeed, it is expected that, in the give and take of litigation, an expert will provide rebuttal testimony that may not be contained in his expert report. *Hochstein v. Microsoft Corp.*, No. 04-cv-73071, 2006 U.S. Dist. LEXIS 74574, at *15 (E.D. Mich. Oct. 13, 2006) (expert declaration “attempting to rebut the analysis of another expert or to clarify his or her position, comporting with the ‘general scheme’ of the [prior] report[s]” is not “‘new.’”). (A1572). Importantly, Williams did not change his underlying infringement theory or opinion in any way. The May 25 Declaration merely explains why the criticism of his opinion misses the mark and does not cause him to change his infringement opinion. This is the opposite of a “new” opinion – it is confirmation that Williams’ opinion was not altered by Soft Gel’s criticism.

The May 25 Declaration did not change in any respect the opinion set forth in Williams' expert report, nor did it offer any new opinion. Williams consistently opined that the Accused Supplements infringe based on the relative ratios of CoQ₁₀

and d-limonene, and comparison of those ratios to the data in FIG. 4. The District Court made an error of law in ruling to the contrary, and accordingly abused its discretion in striking the May 25 Declaration. *Lambright*, 698 F.3d at 820.

3. Williams Was Not Required to Supplement His Reports Under Rule 26(e)

The District Court refused to consider the Williams Declarations under Rule 26(e) because it concluded that they were “supplemental” expert reports and “late filed” with Jarrow’s summary judgment papers. (A27). By its terms, Rule 26(e) applies only where the expert report is “in some material respect . . . incomplete or incorrect.” Fed. R. Civ. P. 26(e)(1)(A). Williams has consistently maintained the same theory of infringement from the disclosure of his report. Because Williams has not changed his theory at all, much less done so in a “material respect,” there was no reason for Williams to supplement his report under Rule 26(e). *Tracinda Corp. v. DaimlerChrysler AG*, 362 F. Supp. 2d 487, 507 & n.6 (D. Del. 2005) (standard for requiring supplementation is whether expert’s opinion was “materially changed”).

As discussed above, the May 4 Declaration did not advance any new opinions or theories of infringement. Williams permissibly elaborated upon and explained the opinions set forth in his expert report. Accordingly, no supplementation under Rule 26(e) was required. *Dow Chem. Co. v. Nova Chems. Corp.*, No. 05-737-JJF, 2010 WL 2044931, at *3 (D. Del. May 20, 2010) (refusing

to strike expert declarations “because they consist of consistent and appropriate elaborations of prior opinions and statements”). (A1580).

Likewise, the May 25 Declaration did not change Williams’ infringement theory or opinion. Defense by an expert of his report in the face of criticism does not render the expert report “incomplete or incorrect”, and an expert may respond to that criticism without supplementing his report. *Hochstein*, 2006 U.S. Dist. LEXIS 74574 at *14-15. (A1572). Indeed, requiring an expert, as a precondition to explanation and defense of his opinions, to address every criticism made by an opposing expert or counsel would lead to an unending battle of supplemental reports, reply reports, and surreply reports. Case law applying the rule logically recognizes that expert reports are not strait-jackets. *Thompson*, 470 F.3d at 1203 (expert not “simply limited to reading his report.”). Accordingly, neither the May 4 Declaration nor the May 25 Declaration was a “supplemental expert report” and Rule 26(e) does not apply.

4. Exclusion of the Williams Declarations Was Harmful, and Will Be Harmful at Trial.

The District Court’s exclusion of the Williams Declarations may not have deprived Jarrow of evidence creating a genuine issue of material fact for trial – because they contained no new opinions and there was other evidence already creating that genuine issue of fact. But it certainly tainted Williams’ opinions in the eyes of the District Court, and it will have the same effect upon the finder of

fact at trial, if not corrected. At trial Williams must be able to explain his opinions and to rebut and defend criticisms of them. Moreover, ¶¶44-73 of the May 4 Declaration are directed to invalidity, and are directly supported in Williams' February 17 and March 15 Rebuttal Reports on invalidity. Compare A630-41 to A425-48 and A463-71. Other than making certain minor corrections in his deposition testimony, Williams' validity opinions set forth in the May 4 Declaration are consistent with his earlier expert report. Although invalidity is not at issue in this appeal, it will likely be at issue on remand, and Williams must be able to defend Soft Gel's criticisms. The District Court's erroneous ruling would leave him tongue-tied. *See Meyer Intellectual Props.*, 690 F.3d at 1376 (exclusion of expert on invalidity was not harmless where the exclusion of testimony made it look as though party had no rebuttal); *Jerden v. Amstutz*, 430 F.3d 1231, 1241 (9th Cir. 2005) (errors in limiting scope of permitted testimony from competing experts were not harmless).

C. The District Court Abused Its Discretion by Excluding the Nazzal Declaration As Undisclosed Expert Testimony

The District Court excluded important fact evidence of a co-inventor when it wrongly concluded that the Nazzal Declaration constituted undisclosed expert evidence. The exclusion of this evidence was harmful to Jarow, and will be harmful at trial.

1. An Inventor May Testify Regarding Personal Knowledge of His Invention

An inventor's testimony concerning what he did to develop or invent the patented technology is fact testimony. "The historical practice has been to treat a witness' factual testimony, *i.e.*, testimony about what a witness did or did not do or observed or did not observe, as not being 'expert' testimony." *Hynix Semiconductor, Inc. v. Rambus, Inc.*, No. C-00-20905-RMW, 2009 WL 230039, at *10 (N.D. Cal. Jan. 27, 2009) (A1589). In fact, an inventor's testimony has been analogized to that of a treating physician, whose testimony is not converted from fact to expert even though derived from specialized education, knowledge and training. *Id.* (A1589-90). It is permissible for "an inventor to describe the process by which he made his discoveries, for an engineer to describe the products he has built, or for a scientist to explain what he knew at a certain point in time. These examples clearly draw on 'technical' knowledge, yet they are not expert testimony." *Id.* (A1590).

Applying the general logic of *Hynix*, courts, including districts courts in the Ninth Circuit, routinely admit inventor testimony as fact or lay witness testimony when it concerns their personal knowledge of their own inventions. *Fresenius Med. Care Holdings, Inc. v. Baxter Int'l, Inc.*, No. C-03-1431, 2006 WL 1330002, at *3 (N.D. Cal. May 15, 2006) (lead engineer, who had not been designated as an expert, permitted to testify as to his personal knowledge of "the machine and the

way that it operates”) (A1601); *Sitrick v. DreamWorks, LLC*, No. CV-03-4265-SVW, 2006 WL 6116641, at *21-22 (C.D. Cal. July 20, 2006) (inventor of product, who had not been designated as an expert, permitted to provide declaration as to the product he invented because he “obviously has sufficient first-hand personal knowledge to state facts regarding [his invention].”) (A1618-19); *see also Irise v. Axure Software Solutions, Inc.*, No. CV-08-03601-SJO (JWJx), 2009 WL 3615075, at *30 n.10 (C.D. Cal. Sept. 11, 2009) (co-creator of alleged infringing computer program, who had not been designated as an expert, permitted to provide declaration in opposition to summary judgment because he had “direct personal knowledge” of the product he created, including its content and functionality, and “the relevant portions of the ... Declaration ... merely describe the [product]....”). (A1667-68). *See also Voice Techs. Grp., Inc. v. VMC Sys., Inc.*, 164 F.3d 605, 615 (Fed. Cir. 1999) (“inventor is a competent witness to explain the invention and ... provide background information, including explanation of the problems that existed at the time the invention was made and inventor’s solution to these problems.”); *Verizon Servs. Corp. v. Cox Fibernet Va., Inc.*, 602 F.3d 1325, 1339-40 (Fed. Cir. 2010) (allowing testimony from the witnesses about the patents they invented based on their personal knowledge).

2. The Nazzal Declaration Presented Fact Evidence, and Should Not Have Been Excluded

The District Court erred, in part, by taking an overly restrictive view of the permissible bounds of inventor testimony based, in part, on a single case that is inconsistent with the logic and weight of the authority cited above, *Baratto v. Brushworks Fine Arts, Inc.*, 701 F. Supp. 2d 1068, 1074 (W.D. Wis. 2010). This restrictive view constituted an error of law and resulted in an abuse of discretion. *Lambright*, 698 F.3d at 820.

In so doing the District Court, without identifying exactly what it was striking, concluded as follows: “Accordingly, all expert testimony proffered by Dr. Nazzal is hereby STRICKEN as untimely.” (A29). At minimum, the District Court appears to have stricken paragraphs 14 and 15 of the Nazzal Declaration. (*Id.*) But careful review of the Nazzal Declaration under the applicable law, including paragraphs 14 and 15, reveals that it presents fact-based evidence from a co-inventor of the ‘786 patent.

Paragraph 1 describes Nazzal’s educational background and experience. (A708).

Paragraph 2 establishes that Nazzal is a co-inventor of the ‘786 patent together with Dr. Mansoor Khan. (*Id.*).

Paragraph 3 describes their discovery in a very general manner, the state of the technology prior to their discovery, and the problems inherent in the existing

technology at the time of the invention; *i.e.*, CoQ₁₀'s poor solubility and tendency to recrystallize. (A708-09).

Paragraph 4 explains the invention. (A709).

Paragraph 5 describes the state of Nazzal's knowledge at the time of the invention. (*Id.*).

Paragraph 6 describes his understanding of why the invention was important. (A709-710).

Paragraph 7 explains what Nazzal invented. (A710).

Paragraph 8 explains the applicable terminology as understood by Nazzal at the time of the invention. (*Id.*).

Paragraph 9 commences Nazzal's description and explanation of the tests employed by him in the inventive process, using FIGS. 1-4 in the '786 patent to illustrate his testimony. Nazzal explains, as a percipient witness, that FIGS. 1 and 3 plot the results of the DSC thermograms used by him ("as employed by me") at the time of the invention to measure the melting points of CoQ₁₀ in the different CoQ₁₀-essential oil mixtures. He then explains the composition of the mixtures that he tested as reflected in the thermograms shown in FIGS. 1 and 3, the known melting point of CoQ₁₀, which he used as a reference point, as well as how the test and reference samples were designed and administered. (A710-11).

Paragraph 10 further explains Nazzal's observation of the DSC tests he administered, as reflected in FIGS. 1 and 3 (using FIG. 3 as an example), including an explanation of the endothermic and exothermic nature of the process as the CoQ₁₀ underwent a phase change from solid to liquid at each melting point. (A711).

Paragraph 11 explains the test and results for the thermogram analysis of a binary mixture of CoQ₁₀ and L-menthol as administered by Nazzal and as reflected in FIGS. 1 and 2. (A711-12).

Paragraph 12 explains the test and results for the thermogram analysis of a binary mixture of CoQ₁₀ and peppermint oil as administered by Nazzal and as reflected in FIG. 3. This is fact evidence notwithstanding that Nazzal, in paragraph 13, appears to be explaining FIG. 3 of the '786 patent. Indeed, it is clear from the Nazzal Declaration as a whole that FIG. 3 results from the test of the binary mixture of CoQ₁₀ and peppermint oil that Nazzal personally administered. *See* Paragraph 9 ("as employed by me"). (A712).

Paragraph 13 explains that the "same procedure" – *i.e.*, a procedure designed by, administered by, and the results observed by, Nazzal – as described in paragraph 12 and reflected in FIG. 3, was followed for binary mixtures of CoQ₁₀ and spearmint oil, lemon oil, and anise oil, with the results plotted on FIG. 4. (A712-13).

Paragraph 14 explains how the invention works, *i.e.*, increasing the amount of lemon oil (and, thus, d-limonene) reduces the melting point of CoQ₁₀; progressively increasing the amount of lemon oil (and, thus, d-limonene) further reduces the melting point. (A713-14). Nazzal's use of the phrase "was observed" in the first sentence of paragraph 14 makes clear that his averments concerning the amount of lemon oil and its effect on the melting point of CoQ₁₀ are based on his personal knowledge. Indeed, Nazzal created the test to prove his hypothesis that increasing the amount of volatile essential oil would further reduce the melting point of the CoQ₁₀. He conducted the test that he created. And the results of the test that he created, as explained in paragraph 14, prove Nazzal's hypothesis.

Accepting that lemon oil is 90% d-limonene, Nazzal made, in paragraph 14, simple mathematical computations converting from a ratio of CoQ₁₀ to lemon oil, to a ratio of CoQ₁₀ to d-limonene. (A713-14). While the Nazzal Declaration does not establish that Nazzal had personal knowledge of the amount of d-limonene in lemon oil, that well understood fact was amply established elsewhere in the record. *See* A596, ¶27 ("As can be seen, lemon oil, which is 90% d-limonene...."); A951 ("To date more than 40 constituents have been identified in [lemon] oil, which contains approximately 90% limonene (by weight)"); A1416 (Soft Gel's submission to the PTO – "contains approx 90% limonene"). Thus, the reduction of the melting point is easily attributed to d-limonene, and Nazzal's reference to the

percentage of d-limonene in lemon oil is harmless because that fact enjoyed so much independent support in the record before the District Court. To hold otherwise -- and to strike paragraph 14 because the Nazzal Declaration did not establish his personal knowledge of the percentage of d-limonene in lemon oil -- elevates form over substance. But even if the references to d-limonene in the Nazzal Declaration, including the mathematical conversions to the amount of d-limonene in each binary mixture of CoQ₁₀ and lemon oil, were stricken, it was still an abuse of discretion for the District Court to strike any other part of paragraph 14 because Nazzal was in all other respects simply explaining his invention based upon his personal knowledge as the inventor. In that regard, paragraph 14 of the Nazzal Declaration presents fact evidence of the inventor that is no different from paragraphs 11 or 12.

Paragraph 15 simply explains Nazzal's invention, which is that a suitable amount of essential oil lowers the melting point of CoQ₁₀, which can then be mixed with other ingredients while maintaining solubility. (A714). This statement is nothing more than an explication of what was invented, from the pen of the inventor. It should not have been stricken by the District Court and it was an abuse of discretion for it to do so.

3. The Fact That Nazzal Was Compensated for His Time Is Irrelevant to the Character of the Evidence Presented by His Declaration

Paragraph 16 of the Nazzal Declaration sets forth the terms on which Nazzal was compensated for his time. (A714). The District Court, in concluding that part of the Nazzal Declaration constituted undisclosed expert testimony, seized upon his compensation as further support for its erroneous conclusion. (A29). But its reliance on his compensation is irrelevant to the analysis.

The compensation of a witness is an ethical matter -- not one that affects the character of a witness's testimony. ABA Formal Ethics Opinion 96-402 provides that:

“[A] lawyer, acting on her client's behalf, may compensate a non-expert witness for time spent in attending a deposition or trial or in meeting with the lawyer preparatory to such testimony, provided that the payment is not conditioned on the content of the testimony and provided further that the payment does not violate the law of the jurisdiction.”

ABA Comm. on Ethics & Prof'l Responsibility, Formal Op. 96-402 (1996).
(A1669).

A year later, the California State Bar reached the same conclusion:

“An attorney may pay a non-expert witness for the time spent preparing for a deposition or a trial, but the attorney must comply with the requirements of rule 5-310(B) of the California Rules of Professional Conduct. Compensation for preparation time or for time spent testifying must be reasonable in light of all the circumstances and cannot be contingent upon the content of the witness’ testimony or on the outcome of the matter.”

Cal. St. Bar Comm'n on Prof'l Responsibility & Conduct, Formal Op. 1997-149 (1997). (A1671).

Thus, whether witnesses are experts is determined from the character of their evidence, not whether they are paid, and it was entirely permissible for Jarrow to compensate Nazzal as a fact witness. Indeed, witnesses are not rendered experts simply because they are paid. *See, e.g., Kirkham v. Société Air France*, 236 F.R.D. 9, 12 (D.D.C. 2006). It was therefore an abuse of discretion for the District Court to premise any determination that Nazzal was an undisclosed expert witness upon the fact that he was compensated. That fact was irrelevant to the inquiry, and it was an abuse of discretion for the District Court to conclude otherwise.

4. Exclusion of the Inventor's Testimony, As Set Forth in the Nazzal Declaration, Was Harmful, and Will Be Harmful at Trial

While the District Court's exclusion of the Nazzal Declaration may not have deprived Jarrow of evidence creating a genuine issue of material fact for trial – because the substance of the declaration appeared elsewhere in the record – it was nonetheless important for Jarrow to have factual testimony in the record from the inventor concerning what he invented, how it works, and why the invention is an important advancement in the art as the inventor understood it at the time of the invention. And on remand it will certainly be important for the jury to hear this

evidence, as a matter of fact, from a co-inventor. The District Court's ruling leaves Jarro without the ability to present this important evidence at trial.

CONCLUSION

Jarrow respectfully requests that the Court reverse the District Court's grant of summary judgment, and:

1. Find that there are disputed issues of fact as to whether the Accused Supplements include a sufficient amount of volatile essential oil to reduce the melting point of ubiquinone to 37°C or below, and remand for further infringement proceedings;
2. Find that the District Court abused its discretion in excluding the May 4 Declaration and the May 25 Declaration, and remand for further infringement proceedings; and
3. Find that the District Court abused its discretion in excluding the Nazzal Declaration, and remand for further infringement proceedings.

Dated: January 10, 2014

McCARTER & ENGLISH, LLP

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ADDENDUM

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JS-6

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FORMULAS, INC.

**UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA – WESTERN DIVISION**

JARROW FORMULAS, INC.,

Plaintiff,

vs.

NOW HEALTH GROUP, INC.

Defendant.

Case No. 2:10-cv-8301-PSG (JCx)

Related Case No. (Consolidated)

2:11-cv-00164 PSG (JCx)

**[PROPOSED] JUDGMENT
FOLLOWING SUMMARY
JUDGMENT RULINGS AND TRIAL**

SOFT GEL TECHNOLOGIES, INC.,

Plaintiff/Counter
Defendant,

vs.

The Honorable Philip S. Gutierrez

Courtroom: Room 880

Location: Roybal Federal Building
255 East Temple Street

[PROPOSED] JUDGMENT FOLLOWING SUMMARY JUDGMENT RULINGS AND TRIAL
CASE NO.: 2:10-CV-8301 PSG (JCX)

ME1 16351523v.2

JARROW FORMULAS, INC.,

Los Angeles, CA 90011

Defendant/Counter

Claimant.

These consolidated cases came before the Court on divers dates in Courtroom 880 of the above-entitled Court as follows:

- on July 31, 2012 in connection with the parties' cross motions for summary judgment, which resulted in the Court's (In Chambers) Order CONSTRUING CLAIMS and GRANTING Defendants' Motion for Summary Judgment (Dkt. #156); and
- on March 12, 13, and June 13, 2013 for a courtside trial, which resulted in the Court's (In Chambers): Findings of Fact and Conclusions of Law Following Bench Trial (Dkt. # 213).

All Parties now having been heard on all outstanding claims and issues and good cause appearing for the entry of judgment,

IT IS HEREBY ORDERED, ADJUDGED AND DECREED that judgment be entered as follows:

1) In favor of NOW Health Group, Inc. d/b/a Now Foods ("NOW") and against Jarro Formulas, Inc. ("JFI"):

(a) As to JFI's Second Amended Complaint against NOW for infringement of U.S. Patent No. 7,588,786 ("the '786 Patent") (Dkt. # 85), for the reasons set forth in the Court's (In Chambers) Order CONSTRUING CLAIMS and GRANTING Defendants' Motion for Summary Judgment (Dkt. #156).

2) In favor of Soft Gel Technologies, Inc. ("Soft Gel") and against JFI:

(a) As to Count I of Soft Gel's First Amended Complaint for Declaratory Judgment (Dkt. # 53) seeking a declaration that the '786 Patent is not infringed, for the reasons set forth in the Court's (In Chambers) Order CONSTRUING CLAIMS and GRANTING Defendants' Motion for Summary Judgment (Dkt. #156);

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[PROPOSED] JUDGMENT FOLLOWING SUMMARY JUDGMENT RULINGS AND TRIAL
CASE NO.: 2:10-CV-8301 PSG (JCX)

ME1 16351523V.2

Case 2:10-cv-08301-PSG-JC Document 217 Filed 09/09/13 Page 5 of 7 Page ID #:4050

Respectfully submitted,

Dated: September 3, 2013

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PROOF OF SERVICE

I am a resident of the State of Connecticut, over the age of eighteen years, and not a party to the within action. I am employed in the office of McCarter & English, LLP which is a member of the bar by pro hac vice of this Court at whose direction the service was made. My business address is McCarter & English, LLP, 185 Asylum Street, Hartford, CT 06103.

On September 3, 2013, I served the following document to all other parties appearing on the docket sheet, as listed below:

[PROPOSED] JUDGMENT FOLLOWING SUMMARY JUDGMENT RULINGS AND TRIAL

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*Counsel for NOW Health Group, Inc.,
 d/b/a NOW Foods*

1
2 I declare under penalty of perjury under the laws of the United States that the
3 above is true and correct. Executed on September 3, 2013, at Hartford, Connecticut.

4
5 /s/ Thomas J. Rechen
6 Thomas J. Rechen
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UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

JS-6 (lc)

CIVIL MINUTES - GENERAL

Case No.	CV 10-8301 PSG (JCx)	Date	August 2, 2012
Title	Jarrow Formulas, Inc. v. Now Health Group, Inc.		

Present: The Honorable Philip S. Gutierrez, United States District Judge

Wendy K. Hernandez

Not Present

n/a

Deputy Clerk

Court Reporter

Tape No.

Attorneys Present for Plaintiff(s):
Not PresentAttorneys Present for Defendant(s):
Not Present

**Proceedings: (In Chambers) Order CONSTRUING CLAIMS and GRANTING
Defendants' Motion for Summary Judgment**

Currently pending before the Court are Plaintiff's and Defendants' proposed *Markman* patent claims constructions and cross-motions for summary judgment. After considering the moving and opposing papers, as well as the arguments made at the July 31, 2012 hearing, the Court hereby construes the contested patent claims and GRANTS Defendants' motion for summary judgment.

I. Background

Jarrow Formulas, Inc. ("JFI") is a manufacturer of nutritional supplements and the holder of U.S. Patent No. 7,588,786 ("the '786 patent"), entitled "Eutectic-Based Self-Nanoemulsified Drug Delivery System." Soft Gel Technologies, Inc. ("Soft Gel") also manufactures nutritional supplements, including the purportedly infringing supplements CoQsol-CF and CoQH-CF (together, the "Accused Supplements"). On November 2, 2010, JFI filed suit against one of Soft Gel's customers, Defendant NOW Health Group, Inc. d/b/a NOW Foods ("NOW"), alleging that NOW had infringed the '786 Patent by offering the Accused Supplements for sale. Soft Gel filed a related action against JFI seeking declarations of patent noninfringement, invalidity, and unenforceability due to inequitable conduct. *See Soft Gel Technologies, Inc. v. Jarrow Formulas, Inc.*, CV 11-0164 PSG (JCx), Docket No. 1 (Jan. 6, 2011); Dkt. # 53. JFI answered and counterclaimed against Soft Gel for infringement and willful infringement. *See id.*, Docket No. 14 (Feb. 2, 2011). The Court consolidated the two cases. *See id.*, Docket No. 39 (May 2, 2011). For ease of reading, the Court will collectively refer to Defendant NOW and Plaintiff/Counter-Claim Defendant Soft Gel as "Defendants," while referring to Plaintiff/Defendant/Counter-Claim Plaintiff JFI simply as "Plaintiff."

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Stated generally, the '786 patent claims an orally-administered dietary supplement comprising ubiquinone and a sufficient amount of a volatile essential oil to reduce the melting point of ubiquinone to 37 C or below, and thereby solubilize the ubiquinone at or below body temperature. Soft Gel and NOW contend that the claims also require that the delivery system be "eutectic-based." See *SG RSUF* ¶ 1. There are three independent claims at issue, namely, Claims 1, 4, and 10, which read as follows:

1. An orally administered dietary supplement including a eutectic-based delivery system, comprising:

a) ubiquinone; and

b) a sufficient amount of a volatile essential oil to solubilize the ubiquinone, and wherein said volatile essential oil is present in a sufficient amount to reduce the melting point of ubiquinone to 37 C or below, and thereby solubilize the ubiquinone comprised in the orally administered dietary supplement at or below body temperature

4. A delivery system for pharmacologically effective agents, comprising:

a) ubiquinone;

b) a surfactant;

c) a sufficient amount of a volatile essential oil to reduce the melting point of ubiquinone to 37 C or below, and thereby solubilize the ubiquinone comprised in the delivery system at or below body temperature.

10. An orally administered dietary supplement including a eutectic-based delivery system, comprising

a) ubiquinone; and

b) a sufficient amount of a volatile essential oil to solubilize the ubiquinone, and wherein said volatile essential oil is present in a sufficient amount to reduce the melting point of ubiquinone to 37 C or below, and thereby solubilize the ubiquinone comprised in the orally administered dietary supplement at or below body temperature; and

c) wherein the dietary supplement composition is contained within a capsule

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Dash Decl., Ex. 1.

According to the '786 patent, "[u]biquinone, also known as Coenzyme Q10 (herein referred to as "CoQ10"), is an important component of the mitochondrial respiratory chain." *Id.* However, because of its poor water solubility, at the time of filing of the '786 patent ubiquinone presented a challenge when developing a formulation for oral administration. *See id.* Traditional methods involved dissolving the CoQ10 in a fixed oil, which was then blended with a suitable solubilizing agent. *Id.* Due to the limited solubility of CoQ10 in these oils, such methods often resulted in low drug loading and suffered from re-crystallization of the CoQ10. *See id.* The '786 patent attempted to solve this problem by describing "a eutectic-based semisolid self-nanoemulsified drug delivery system (SNEDDS) [] as an alternative to the conventional self-emulsifying vehicles." *See id.* 2:32-35. "In a eutectic-based SNEDDS, the melting point depression method allows the oil phase containing the drug itself to melt at body temperature from its semisolid consistency and disperse to form emulsion droplets in nanometer size range." *Id.* 2:55-61. As recited in the specification:

The present invention is directed to a eutectic-based self-nanoemulsified drug delivery system...containing an isotropic mixture of oil, surfactant, co-surfactant and a pharmacologically effective drug. The oil present in the SNEDDS is an essential oil that is a volatile oil, preferably selected from the group comprising menthol, spearmint oil, peppermint oil, lemon oil, anise oil and mixtures thereof. The essential oils in the SNEDDS are present in a preferred amount of 19-26 wt. %. The pharmacologically effective drug present in the SNEDDS is...[m]ost preferably [] ubiquinone (hereinafter referred to as "CoQ10")...the preferred amount of the pharmacologically effective drug in the SNEDDS is 19-26 wt. %. [When combined with the preferred amount of the preferred surfactant and cosurfactant, the] SNEDDS produces a semi-solid mass which is filled into soft or hard gelatin capsules.

Id. 4:24-54.

It is undisputed that one of the Accused Supplements, CoQsol-CF, includes ubiquinone. The second Accused Supplement, CoQH-CF contains ubiquinol. The parties agree that ubiquinol is "a reduced form of ubiquinone," *see SG SUF* ¶ 26, however, they dispute whether "ubiquinone" as claimed in the '786 patent may be construed to cover supplements containing ubiquinol.

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Now before the Court are Defendants' motion for summary judgment of noninfringement and invalidity and JFI's motion for partial summary judgment of infringement of claims 1, 8, 10, and 12, validity of the asserted claims, and no inequitable conduct. *See* Dkt. # 98, 100-1, 113. In order to determine whether the '786 patent is infringed or invalid, however, the Court must first construe the claims.

II. Claim Construction

The parties have not filed a Joint Claim Construction Statement. From the briefing, the Court has gleaned the following disputed terms:

- (1) whether the preamble term "a Eutectic-Based Delivery System" limits the Claims
- (2) "Melting Point"
- (3) "Ubiquinone"

A. Legal Standard for Claim Construction

"[T]he interpretation and construction of patent claims, which define the scope of the patentee's rights under the patent, is a matter of law exclusively for the court." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 970-71 (Fed. Cir. 1995), *aff'd*, 517 U.S. 370, 116 S. Ct. 1384, 134 L. Ed. 2d 577 (1996).

Also, the Federal Circuit has "frequently stated that the words of a claim are generally given their ordinary and customary meaning." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc), *cert. denied*, 546 U.S. 1170, 126 S. Ct. 1332, 164 L. Ed. 2d 49 (2006) (citation omitted). In fact, "the construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." *Id.* at 1324.

The "ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Id.* at 1313 (citation omitted). "The inquiry into how a person of ordinary skill in the art understands a claim term provides an objective baseline from which to begin claim interpretation." *Id.* (citation omitted). "That starting point is based on the well-settled understanding that inventors are typically persons skilled in the field of the invention and that patents are addressed to and intended to be read by others of skill in the

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pertinent art.” *Id.* (citation omitted). “Importantly, the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification.” *Id.*

In some cases, the ordinary meaning of claim language as understood by a person of skill in the art may be readily apparent even to lay judges, and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words. In such circumstances, general purpose dictionaries may be helpful. In many cases that give rise to litigation, however, determining the ordinary and customary meaning of the claim requires examination of terms that have a particular meaning in a field of art. Because the meaning of a claim term as understood by persons of skill in the art is often not immediately apparent, and because patentees frequently use terms idiosyncratically, the court looks to those sources available to the public that show what a person of skill in the art would have understood disputed claim language to mean. Those sources include the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art.

Id. at 1314 (internal citations and quotation marks omitted).

While considering the allowable sources of evidence to construe patent claims, a Court must consider the hierarchy of importance that the Federal Circuit has created for those sources of evidence. First, “the context in which a term is used in the asserted claim can be highly instructive.” *Id.* at 1314. Also, the Federal Circuit has made clear that claims “must be read in view of the specification, of which they are a part. ... [T]he specification is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term.” *Id.* at 1315 (internal citation and quotation marks omitted). Furthermore, although the prosecution history “often lacks the clarity of the specification and thus is less useful for claim construction purposes,” *id.* at 1317, it should also be considered and given great weight as “intrinsic evidence.” *Id.* Finally, a Court may consider “extrinsic evidence, which consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises.” *Id.* (citation and internal quotation marks omitted). However, while extrinsic evidence can shed useful light on the relevant art, it is less significant than the intrinsic record in determining the legally operative meaning of claim language. *Id.*

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Finally, because of the importance of the specification in construing claim terms, the Federal Circuit's "cases recognize that the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Id.* at 1316. There is no longer a "heavy presumption" that the ordinary meaning of patent terms to one schooled in the art governs, nor is it necessary to show that the specification contains an "explicit definition" of a claim term. Rather, it is appropriate for the Court to depart from the "ordinary" meaning of a disputed term where the intrinsic evidence persuasively demonstrates "what the inventors actually invented and intended to envelop with the claim." *Id.* at 1316. However, "[t]hat claims are interpreted in light of the specification does not mean that everything expressed in the specification must be read into all the claims." *SRI Int'l v. Matsushita Elec. Corp.*, 775 F.2d 1107, 1121 (Fed. Cir. 1985) (citation omitted). Thus, "although the specification often describes very specific embodiments of the invention, [the Federal Circuit has] repeatedly warned against confining the claims to those embodiments." *Phillips*, 415 F.3d at 1323.

B. The Court's Construction of the Claims

The Court begins by noting that the '786 patent's effective filing date is December 14, 2001, *i.e.*, the filing date of U.S. Provisional Patent Application No. 60/331,292 ("the '292 Application"), to which the '786 patent claims priority. *See Dash Decl.*, Ex. 9 ¶ 17. The parties agree that the person of ordinary skill in the art is a PhD-level or doctoral candidate pharmaceutical researcher; accordingly, the claims are properly construed from the perspective of such person circa December 14, 2001. *See Grondahl Decl.*, Ex. LL. With this in mind, the Court construes the disputed claim terms as follows:

1. The Preamble Term "Eutectic-Based Delivery System" Does Not Limit the Claims

The parties dispute whether the term "eutectic-based delivery system" is simply a descriptive term for the invention set forth in the bodies of the claims, or is a limitation. "Whether to treat a preamble as a limitation is a determination resolved only on review of the entire patent to gain an understanding of what the inventors actually invented and intended to encompass by the claim." *Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 808-10 (Fed. Cir. 2002) (quoting *Corning Glass Works v. Sumitomo Electric U.S.A., Inc.*, 868 F.2d 1251, 1257 (Fed. Cir. 1989) (quotations and alterations omitted). "In general, a preamble limits the invention if it recites essential structure or steps, or if it is 'necessary to give life, meaning, and vitality' to the claim." *Id.* (quoting *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305 (Fed. Cir. 1999)). "Conversely, a preamble is not limiting 'where a patentee

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presently described eutectic reaction indicates that there has been a change or modification of the physical properties of ubiquinone; *i.e.*, depression of its melting point....Shapira does not teach...a eutectic-based delivery system comprising ubiquinone and a sufficient amount of a volatile oil or volatile ingredient of an essential oil to solubilize and reduce the melting temperature of ubiquinone to 37 C or below.”).

The Court rejects Defendants’ proposed construction because a review of the intrinsic evidence demonstrates that the inventors used the terms “eutectic” and “eutectic-based” more broadly to describe mixtures in which only the melting point of one ingredient - ubiquinone - had been reduced. First, a strict definition of “eutectic” or “eutectic-based” would exclude embodiments and recitations disclosed in the ‘786 patent. “We normally do not interpret claim terms in a way that excludes disclosed examples in the specification.” *Verizon Servs. Corp. v. Vonage Holdings Corp.*, 503 F.3d 1295, 1305 (Fed. Cir. 2007). For example, FIG. 4 of the ‘786 patent demonstrates a binary phase diagram of CoQ10 and various essential oils. The specification recites that these compounds “formed binary eutectic systems,” despite the fact that only “a gradual decrease in the melting temperature of CoQ10” was observed, such that “it [became] feasible to convert CoQ10 into an oily phase at or below body temperatures.” See ‘786 patent, 6:33-40. Moreover, it is undisputed that the melting points of some of the essential oils disclosed in FIG. 4 are below the melting points of the recited mixtures.² Therefore, under Defendants’ proposed construction of “eutectic,” these embodiments would be excluded. The prosecution history is in accord with this broader construction: “a eutectic effect represents a change or modification of the physical properties *in at least one of the components* – demonstrated by the observed reduction in the melting point.” See *Dash Decl.*, Ex. 18, p. 10 (Response of March 11, 2009).

With this definition in mind, the “eutectic-based” language in the preamble is merely duplicative of the melting point reduction limitation contained in the body of the claims. Where the preamble “is reasonably susceptible to being construed to be merely duplicative of the limitations in the body of the claim (and was not clearly added to overcome a rejection), we do not construe it to be a separate limitation.” *Symantec Corp. v. Computer Associates Intern., Inc.*, 522 F.3d 1279, 1288-89 (Fed. Cir. 2008). And while Defendants place considerable emphasis on a March 11, 2009 Response in which the Applicant distinguished two prior art references for failing to disclose a “eutectic-based delivery system” or a “eutectic mixture;” a review of the Response as a whole shows that the Applicant was concerned with distinguishing the prior art based on “one of the claim limitations, specifically, ‘a sufficient amount of an essential oil...to reduce the melting point of ubiquinone to 37 C or below,’ and not based on the preamble. See

²As noted, d-limonene, a component of lemon oil, has a melting point of around -96 C.

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Dash Decl., Ex. 18, p. 6. The Applicant's references to a "eutectic-based delivery system," "eutectic effect," and "eutectic reaction," which are followed closely by references to the melting point reduction limitation, *see id.* p.7 ("the presently described eutectic reaction indicates that there has been a change or modification of the physical properties of ubiquinone; i.e., depression of its melting point"); p.10 ("[t]he dietary supplement eutectic mixture of claim 1, as amended, comprises ubiquinone and a sufficient amount of a volatile oil or volatile ingredient of an essential oil in order to observe the eutectic effect; i.e., to depress the melting temperature of ubiquinone to 37 C or below, resulting in ubiquinone being solubilized into the oily phase of the mixture"), are properly construed as a short-hand descriptor for this limitation. Moreover, the Applicant stated in other correspondence that the preamble was not a limitation, and the Examiner, too, expressed an understanding that it was merely an "intended use" already "inherent in the referenced composition." *See Sankaran Decl.*, Ex. 50, p.3; *Grondahl Decl.*, Ex. E ("applicant does not intend by this amendment to represent or otherwise imply that the preamble should be considered a limitation of the claims.").

In sum, the preamble merely gives a descriptive name – i.e., "eutectic-based" – to the melting point reduction limitation set forth in the bodies of the claims. It adds nothing to their structures or steps. Further, the Applicant's references to "eutectic-based" fail to evidence clear reliance on the preamble, as opposed to the claim limitations themselves. Accordingly, the general rule that the preamble is not limiting applies. *See Catalina*, 289 F.3d at 808.

2. "Melting Point" (in all asserted claims)

JFI's Proposed Construction	Defendants' Proposed Construction
The temperature at which CoQ10 is liquid in essential oil	The temperature at which a chemical agent has a transition from solid to liquid due to the application of heat

The Court construes the term "melting point" to mean "the temperature at which a chemical agent has a transition from solid to liquid due to the application of heat." The Court bases its construction on the patent specification and the ordinary usage of the term. The specification refers to "melting temperature" as the temperature at which "it becomes feasible to

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convert CoQ10 into an oily phase.” See ‘786 patent, 6:35-40. In accordance with Defendant’s proposed construction, it therefore contemplates the specific temperature at which the physical change of the substance from its solid to its liquid phase occurs, rather than a continuum of temperatures at which the substance “is liquid.” Moreover, Example 1 discloses illustrations in which CoQ10 mixtures were “melted” at 37 C, and therefore contemplates the application of temperatures sufficient to bring about the physical change, *i.e.*, “heat.” See *id.* 5:45-7:16. Likewise, both experts agree that the ordinary meaning of the term “melt” is “a phase transition from solid to liquid” through the application of heat. See *Dash Decl.*, Ex. 3, at ¶ 38; *Sankaran Decl.*, Ex. 21 (Williams Depo. 42:22-43:6). Reliance on expert testimony is appropriate where the terms at issue are technical terms. *Phillips*, 415 F.3d at 1317-18. The ‘786 patent otherwise provides no basis to conclude that the inventor acted as his own lexicographer or intended the term melting point to have anything other than its ordinary meaning.³

Relatedly, the parties also dispute whether “melting” as used in the ‘786 patent is synonymous with “dissolve” or “solubilize.” Defendants contend that the terms are not synonymous to one of ordinary skill in the art, and that while the Accused Supplements *dissolve* ubiquinone and ubiquinol in d-limonene, there is no evidence that the melting points of ubiquinone or ubiquinol have been reduced. Dr. Alekha Dash, Defendants’ expert, opines that while ubiquinone readily dissolves in d-limonene, “[b]y requiring the essential oil to reduce the

³Initially, the Court was convinced by Plaintiff’s argument that requiring the change to occur “due to the application of heat” would improperly exclude certain disclosed embodiments. As the Court noted above, “a claim interpretation that excludes a preferred embodiment from the scope of the claim is rarely, if ever, correct.” *On-Line Techs., v. Bodenseewerk Perkin-Elmer GmbH*, 386 F.3d 1133, 1138 (Fed. Cir. 2004). Specifically, the binary phase diagram showing the melting points of mixtures of ubiquinone and various essential oils disclosed in FIG. 4 of the ‘786 patent includes some mixtures that melt below room temperature. See ‘786 patent, 6:33-37. For example, 70:30 and 80:20 mixtures of anise oil:ubiquinone melt at between 16 C and 18 C. See ‘786 patent, FIG. 4. The Court was thus concerned that mixing these components in the specified percentages at ambient temperature would achieve the desired melt without someone performing the additional step of physically “applying heat” to the mixture, and would therefore be excluded under Defendants’ proposed construction. However, Defendants clarified at the hearing that the “application of heat” was not necessarily a separate step to be performed in all cases. Rather, “application of heat” requires only the presence of a sufficient temperature to work the physical change. Therefore, where a substance melts below room temperature, as in the embodiments discussed *supra*, the ambient temperature itself supplies the requisite “application of heat.” Accordingly, nothing in the patent warrants departure from the ordinary meaning of the term as set forth above.

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melting point, the claims make clear that the mechanism for making CoQ10 available is by melting it to a liquid phase. However, to a person of ordinary skill in the art, melting is different from dissolving.” *See Dash Decl.*, Ex. 3, ¶ 45. According to Dr. Dash, subsequent doctoral-level research undertaken by Dr. Mansoor Khan, one of the inventors of the ‘786 patent, demonstrates both that “melting” and “dissolving” are not synonymous, and that d-limonene does not lower the melting point of ubiquinone. *See id.* ¶ 47.

Plaintiff’s position on whether “melting” is synonymous with “dissolving” is somewhat of a moving target, even at this late stage in the litigation. The Court first notes that JFI’s current proposed construction of “melting point” – *i.e.*, the temperature at which CoQ10 *is liquid* in essential oil – is broad enough to encompass mixtures in which the ubiquinone has been dissolved, solubilized, *or* melted in the essential oil. As disclosed by Plaintiff’s expert, Dr. Williams, in an untimely March 15 Supplemental Rebuttal Report on invalidity, Plaintiff’s construction until that time was that the inventors used the terms “melting,” “dissolution,” and “solubilization” interchangeably. *See Dash Decl.*, Ex. 9, ¶ 19 (“As used in the ‘786 patent, the term ‘melting’ refers to the process and/or state wherein the CoQ10 crystals dissolve or are solubilized into solution. Thus, the ‘786 patent teaches that the eutectic mixture provides for the solubilization (*i.e.*, dissolution) of higher amounts of ubiquinone without requiring heating to high temperatures.”); ¶ 27 (“the specification and file history of both the ‘786 patent and the ‘406 application indicate that the inventors use the term ‘melting’ interchangeably with dissolution or solubilization. Therefore, it is my opinion that the person of skill in the art at the time of the invention claimed by the ‘786 patent would have understood that the inventors use the term ‘melting’ to describe the process of CoQ10 being solubilized or dissolved by a volatile essential oil.”).

In fact, citing to the Applicant’s arguments during prosecution, Dr. Williams expressly disagreed with Dr. Dash’s construction of “melting” as requiring a transition of the ubiquinone to its liquid phase independent of its dissolution in the essential oil on the grounds that “the inventors stated that, ‘[a]s taught and described by the present specification, CoQ10 is dissolved or melted in the volatile essential oil...the specification teaches and describes that CoQ10 is dissolved or solubilized by the volatile essential oil, forming a single, isotropic or homogeneous oily (*i.e.*, hydrophobic) phase...In other words, no aqueous phase exists in the system resulting from performance of the claimed methods.” *Id.* ¶ 26. Dr. Williams reiterated this position at his deposition taken on April 11, 2012, at which time he stated that while outside the context of the ‘786 patent, “‘melt’ would be understood by a person of ordinary skill in the art to [] mean a phase transition from a solid to a liquid,” *see Dash Decl.*, Ex. 21, 29:3-6, reading the patent as a

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First, the claims require that the volatile essential oil “is present in a sufficient amount to reduce the melting point of ubiquinone to 37 C or below, *and thereby solubilize* the ubiquinone” at or below body temperature. Second, the written description of the ‘786 patent distinguishes traditional methods of preparation in which “active ingredients are dissolved in fixed oils or triglycerides and subsequently blended with suitable solubilizing agents” from the claimed melting point reduction method. *See* ‘786 patent, 1:55-59. The fact that the melting point reduction is used as a means to solubilize or dissolve and as a basis for distinguishing traditional methods indicates that melting is distinct from dissolving or solubilizing. Moreover, the specification as a whole is concerned with addressing the problem that ubiquinone is difficult to dissolve, and proposes the melting point reduction method as a solution to this problem. *See id.* 1:59-60; 6:57-60. Thus, the inventors knew what it meant to dissolve ubiquinone, and could have described and claimed the invention as “dissolving” ubiquinone if that is what they thought they invented. Instead, the written description and claims define the invention not as dissolving ubiquinone, but as reducing its melting point: “Due to the limited solubility of CoQ10 in fixed oils and triglycerides, the melting point depression method using essential oils provides an attractive alternative for the preparation of an emulsified formulation.” *See id.* 6:57-60.

Third, the specification refers to a physical change in the ubiquinone and to the formation of an “oily melt.” *See* ‘786 patent, 6:11-27 (emphasis added) (discussing the ubiquinone:1-menthol mixture and noting that the “volatile ingredients of menthol are responsible for the *physical changes* in CoQ10, i.e. depression of its melting temperature”); 6:38-40 (describing the effect of the embodiments disclosed in FIG. 4 as “convert[ing] CoQ10 into an oily phase.”). It does not discuss dissolution.

Fourth, a distinction between “melting” and dissolving is in accord with statements made by the Applicant during prosecution to distinguish the prior art. The Applicant emphasized that “the presently described eutectic reaction indicates that there has been a change or modification of the physical properties of ubiquinone; i.e., depression of its melting point.” *Dash Decl.*, Ex. 18 (Response of March 11, 2009), p. 7. The Applicant also distinguished several prior art references on the grounds that while the prior art recited compositions that included ubiquinone and essential oil, they did not disclose a eutectic or melting point reduction in the ubiquinone. *See Sankaran Decl.*, Ex. 29. The Court agrees that having taken the position in prosecution that the claims are directed to a change in the physical properties of ubiquinone, JFI cannot now strike the melting point reduction limitation from the claims and replace it with “dissolve.” *See Chef Am., Inc. v. Lamb-Weston, Inc.*, 358 F.3d 1371, 1372, 1372 (Fed. Cir. 2004) (holding that the “claim means what it says,” and that while it could easily have been written to reflect patentee’s proposed construction, “the court cannot rewrite it.”).

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A non-moving party who bears the burden of proving at trial an element essential to its case must sufficiently establish a genuine dispute of fact with respect to that element or face summary judgment. *See Celotex Corp. v. Catrett*, 477 U.S. 317, 322-23, 106 S. Ct. 2548, 91 L. Ed. 2d 265 (1986). Such an issue of fact is a genuine issue if it reasonably can be resolved in favor of either party. *See Anderson*, 477 U.S. at 250-51. If the moving party seeks summary judgment on a claim or defense for which it bears the burden of proof at trial, the moving party must use affirmative, admissible evidence. Admissible declarations or affidavits must be based on personal knowledge, must set forth facts that would be admissible evidence at trial, and must show that the declarant or affiant is competent to testify as to the facts at issue. *See Fed. R. Civ. P. 56(e)*.

B. Infringement/Non-Infringement

For a finding of patent infringement, each limitation of a claim must be found in the accused infringing product, either literally or under the doctrine of equivalents. *See Jeneric/Pentron, Inc. v. Dillon Co., Inc.*, 205 F.3d 1377, 1382-83 (Fed. Cir. 2000); *see generally Warner-Jenkinson Co., Inc. v. Hilton Davis Chem. Co.*, 520 U.S. 17 (1997). An accused product infringes literally when “every limitation recited in the claim appears in the accused product, i.e., the properly construed claim reads on the accused product exactly.” *Jeneric/Pentron*, 205 F.3d at 1382. A product infringes under the doctrine of equivalents if it contains “each limitation of the claim or its equivalent.” *Id.* at 1383; *see also Warner-Jenkinson*, 520 U.S. at 29 (noting that “the doctrine of equivalents must be applied to individual elements of the claim, not to the invention as a whole”). “An element in the accused product is equivalent to a claim element if the differences between the two are ‘insubstantial’ to one of ordinary skill in the art.” *Jeneric/Pentron*, 205 F.3d at 1383 (citation omitted).

Defendants move for summary judgment on all 13 claims in the ‘786 patent. As noted, the ‘786 patent encompasses three independent and ten dependent claims. The melting point reduction limitation is shared by all three independent claims; accordingly, if Plaintiff fails to raise a triable issue of fact regarding whether the Accused Supplements reduce the melting point of ubiquinone to 37 C or below, Defendants are entitled to summary judgment on all 13 claims.

Plaintiff performed no independent analysis of the Accused Supplements. Rather, Plaintiff’s expert, Dr. Williams, took the position that melting was synonymous with dissolving within the meaning of the ‘786 patent, and then concluded that because Soft Gel advertises that the Accused Supplements are completely dissolved at room temperature, the melting point reduction limitation was satisfied by necessity. *See Dash Decl.*, Ex. 9, ¶ 36. Much of the evidentiary basis for Dr. Williams’ February 10 Supplemental Expert Disclosure Report and

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accompanying Claim Comparison Chart is irrelevant upon a proper construction of the melting point reduction limitation. *See Dash Decl.*, Ex. 4, ¶¶ 24-25 (Soft Gel and NOW “extensively promote that the [Accused Supplements] are ‘Crystal-Free’ and ‘100% Solubilized;’” these advertisements “say nothing about requiring heating in order to solubilize (dissolve) the ubiquinone;” Soft Gel has stated to the USPTO that the “ubiquinone contained in [its] soft gelatin capsules remains solubilized at ambient temperatures, without the need for heat, when combined with a sufficient amount of d-limonene.”); *accord* Ex. 5.

And while Dr. Williams’ Report also opines in a single paragraph that upon “an analysis of SGTI’s Formulation Cost Sheets...the amounts by weight of ubiquinone and limonene utilized in the formulations would be within the eutectic range as described by the ‘786 patent,” *see Dash Decl.*, Ex. 4, ¶ 26, the March 15 Supplemental Report and Dr. Williams’ deposition make clear that his opinion in this regard was still rooted in the faulty premise that the melting point reduction limitation required only that the ubiquinone be in a liquid state at or below 37 C. *See SG MSJ*, 12:7-14; *Dash Decl.*, Ex. 9, ¶¶ 27, 36 (reasoning that Soft Gel’s own products and the ‘786 patent teach that “a sufficient amount of a volatile essential [oil] can and does solubilize CoQ10 and maintain its solubility at temperatures of 37 C or below, or, *in the terms of the ‘786 patent*, reduces its melting temperature”); *Sankaran Decl.*, Ex. 21 (Williams Depo., 187:3-21).

This opinion was also based upon an incomplete ingredient list for the Accused Supplements. *See Dash Decl.*, Ex. 3, ¶ 62; Ex. 22. During prosecution of the ‘786 patent and in opposition to Defendants’ motion for summary judgment on invalidity the Applicant and Plaintiff stressed that eutectic mixtures cannot be predicted, but must be determined empirically by mixing two or more ingredients and assaying for a reduction in the melting temperature. *See, e.g., Dash Decl.*, Ex. 3, ¶ 58 (“As is well known in the art, eutectic mixtures cannot be predicted, and therefore, generally must be identified empirically. Therefore, even if *at the time of the invention* a eutectic mixture had been demonstrated for another quinone, which it was not, a reasonable likelihood of success did not exist with respect to the combination of CoQ10 and an essential oil.” Amendment and Response of January 15, 2008); ¶ 59 (“A eutectic effect cannot be predicted, *a priori*, but is empirically determined by mixing two or more ingredients and assaying for a reduction in the melting temperature.” RCE and Amendment of August 6, 2008); *Sankaran Decl.*, Ex. 49 (“the eutectic effect does not necessarily and inevitably occur merely from the presence of the two ingredients (i.e., an essential oil and ubiquinone) in a mixture. Significantly, the eutectic effect does not necessarily occur merely because CoQ10 and an essential oil are present at equal amounts in a mixture. *As taught in the present specification*, a eutectic composition is dependent on the relative proportions of all ingredients in the mixture.” Response of March 11, 2009) (italics added, underlining in original).

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At his deposition, Dr. Williams agreed that eutectic mixtures cannot be predicted, do not necessarily occur simply because CoQ10 and an essential oil are present in equal amounts in a mixture, and that “as taught in the present specification, a eutectic composition is dependent on the relative proportion of all ingredients in the mixture.” *See Sankaran Decl.*, Ex. 21 (Williams Depo. 190:2-191:4). Nonetheless, at the time he issued his reports and prior to his deposition, Dr. Williams had not reviewed the detailed product formulations and manufacturing methods provided by Soft Gel. *See id.* 176:8-177:24. Nor did Dr. Williams perform any independent testing or assays on a mixture including all the ingredients of any accused product. Instead, Dr. Williams calculated a binary ubiquinone:d-limonene mixture from the percentages disclosed in the Formulation Cost Sheets and then extrapolated from the FIG. 4 data points to determine the temperature at which that binary mixture would melt.⁶ *See id.* 180:8-187:2. It is undisputed, however, that FIG. 4 pertains to binary mixtures only, and that the Accused Supplements are not binary mixtures. Dr. Williams twice admitted that he did not take all the ingredients of the Accused Supplements into account and only considered a binary mixture of ubiquinone and d-limonene:

Q: So you didn’t take into account the other ingredients?

A: I think I didn’t. I think I didn’t.

Id. 187:3-5.

Q: Okay. In the percent calculation that you did to compare to Paragraph 4, you would have only taken into account just the weights of CoQ10 and limonene, wouldn’t you?

A. In that – for that comparison with Figure 4, probably so.

Id. 192:12-17; *accord* 186:4-187:5.

Finally, when pressed to explain the inconsistency in his conflicting positions that eutectic compositions cannot be predicted and are dependent on the relative proportion of *all* ingredients, and yet he could determine that the Accused Supplements were the product of a eutectic mixture simply by comparing the percentages of two of their ingredients with the binary melting points disclosed in FIG 4, Dr. Williams clarified that his opinion in this regard was still

⁶FIG. 4 discloses the melting points of lemon oil:ubiquinone mixtures at various ratios.

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based on a construction of the “melting point reduction” limitation that was satisfied simply by virtue of the ubiquinone *being liquid* at or below 37 C:

Q: But, then, how can you predict it’s a eutectic without taking into account the other ingredients?

A: You know, I just – I can’t quite remember sitting here right now. I mean, I’m – I’m reading what I remember doing, and – that’s what I’ve done. And – and that – I mean, it supports what I’ve already said here. *I mean, this point is about it being dissolved. And the point is, is here they’re advertising a product that’s 100 percent solubilized, crystal-free, assuming that’s sitting on the shelf. [] I looked at patents and – and patent application from SGTI. And from those CoQ10 is dissolved in d-limonene. So, I mean, I’m – I’m putting together the different pieces saying that basically at – at room temperature this formulation, it exists as a solution.*

Id.

Thus, at the time the opening briefs on summary judgment were filed, while it was undisputed that the Accused Supplements were “crystal free” at room temperature, JFI had adduced *no evidence* to support that this was due to a reduction in the melting temperature of ubiquinone, and thus that this limitation of the ‘786 patent was met. Further, all of JFI’s disclosures pointed toward a claim construction stance that effectively read the melting point reduction limitation out of the claims by maintaining that this limitation was satisfied whenever the ubiquinone was dissolved or stayed liquid in essential oil at 37 C or below. Recognizing this, Defendants brought a motion for summary judgment on patent invalidity tailored to this interpretation, a claims construction motion designed to rebut it, and a motion for summary judgment of non-infringement premised on Plaintiff’s failure to adduce any evidence to support infringement under a proper construction of the melting point reduction limitation.

In connection with its motion for summary judgment and in opposition to Defendants’, JFI not only reversed tack on its claim construction position, it submitted *three additional expert reports*; two more from Dr. Williams, and a third from Dr. Sami Nazzal, who was not previously disclosed as an expert. Defendants object to these belated and improper expert disclosures, and move that they be stricken under Rule 37(c)(1).

1. Defendants’ evidentiary objections to Plaintiff’s Expert Disclosures

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“Evidentiary rulings are procedural matters that do not raise issues unique to patent law,” therefore the Court applies the law of the “appropriate regional circuit” to the determination. *Chimie v. PPG Industries, Inc.*, 402 F.3d 1371, 1376 (Fed. Cir. 2005). Rule 26 requires parties to disclose all expert evidentiary material that may be relied upon at trial, and further provides that these disclosures be made at the times directed by the court. Fed. R. Civ. P. 26(a)(2)(C). Expert disclosures must include “a complete statement of all opinions the witness will express and the basis and reasons for them” and “the facts or data considered by the witness in forming them.” See Fed. R. Civ. P. 26(2)(B)(ii). Moreover, pursuant to Rule 26(e), a party is under a duty to supplement a Rule 26(a) expert report “if the party learns that in some material respect the disclosure or response is incomplete or incorrect, and if the additional or corrective information has not otherwise been made known to the other parties” Fed. R. Civ. P. 26(e). “Rule 37(c)(1) gives teeth to these requirements by forbidding the use at trial of any information required to be disclosed by Rule 26(a) that is not properly disclosed.” *Yeti by Molly Ltd. v. Deckers Outdoor Corp.*, 259 F.3d 1101, 1106 (9th Cir. 2001). This rule excludes untimely expert witness testimony, unless the “part[y’s] failure to disclose the required information is substantially justified or harmless.” *Id.* Furthermore, a party that fails to comply with a scheduling order is subject to the sanctions available to a court to enforce its orders, including those authorized by Rule 37(b)(2)(A)(ii)-(vii). Fed. R. Civ. P. 16(f).

The Court’s Scheduling Order set January 20 and February 17 as the dates for disclosure of opening and rebuttal expert reports, respectively. See Dkt. # 43. On January 19, the Court denied a joint request to extend the expert disclosure dates. Dkt. # 90. Soft Gel complied and provided a timely expert report addressing invalidity on January 20. However, JFI did not produce its initial expert report until February 10. Both parties’ rebuttal reports were timely filed on February 17.

JFI then commenced a string of improper exchanges, beginning with a “Supplemental Rebuttal” report from Dr. Williams offered on March 15. Pursuant to the Court’s Scheduling Order, Expert Discovery closed on April 15, 2012. Nonetheless, JFI offered two more “supplemental” Williams declarations after this date. One was filed simultaneously with JFI and Defendants’ opening briefs on summary judgment on May 4, 2012, which was also the last day to file motion. Plaintiff also filed the declaration of Dr. Sami Nazzal at this time. Incredibly, Plaintiff then filed a second “supplemental” Williams Declaration on *May 25th*. In other words, JFI filed its *fifth* untimely expert report on the same day that Defendants’ opposition to its motion for summary judgment was due, more than three months after the deadline for disclosing opening and rebuttal expert reports had passed, and over a month after expert discovery had closed.

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Defendants object to the consideration of all three untimely Williams “supplemental” reports on the grounds that they express new and deeper opinions beyond the scope of a proper supplemental disclosure. They also object to the Court’s consideration of the Nazzal Declaration as Dr. Nazzal was not disclosed as an expert. As far as Defendants’ objection to the March 15 “Supplemental Rebuttal” report is concerned, that objection is **OVERRULED** on the grounds that because the report was served four weeks before Dr. Williams’ deposition, Defendants had ample opportunity to review the report and question Dr. Williams regarding its contents, and therefore have not been prejudiced. However, for the following reasons the Court agrees that the May 4 and May 25 supplemental Williams declarations and the Nazzal Declaration are improper supplemental disclosures that must be stricken.

Although Rule 26(e) obliges a party to “supplement or correct” its disclosures upon information later acquired, this “does not give license to sandbag one’s opponent with claims and issues which should have been included in the expert witness’ report (indeed, the lawsuit from the outset). To rule otherwise would create a system where preliminary reports could be followed by supplementary reports and there would be no finality to expert reports” *Beller ex. rel. Beller v. United States*, 221 F.R.D. 696, 701 (D.N.M. 2003). Enabling this pattern of behavior “would surely circumvent the full disclosure requirement implicit in Rule 26 and would interfere with the Court’s ability to set case management deadlines.” *Id.* at 701-02. Accordingly, a supplemental expert report that states additional opinions or “seeks to ‘strengthen’ or ‘deepen’ opinions expressed in the original expert report” is beyond the scope of proper supplementation and subject to exclusion under Rule 37(c). *Cohlmia v. Ardent Health Servs., LLC*, 254 F.R.D. 426, 433 (N.D. Okla. 2008).

Plumley v. Mockett, 2010 WL 8160423, at *4 (C.D. Cal. May 26, 2010).

“Supplemental” reports which provide new opinions designed to strengthen the proffering party’s legal arguments are improper under Rule 26(e). *See id.* (citing *Solaia Tech. LLC v. ArvinMeritor, Inc.*, 361 F.Supp.2d 797, 807 (N.D. Ill. 2005) (“If the late-filed opinions are new, they must be stricken.... Thus, the Court’s first step is to determine whether the statements by [the expert] are new or contradictory opinions.”). “Excluding expert evidence as a sanction for failure to disclose expert witnesses in a timely fashion is automatic and mandatory unless the party can show the violation is either justified or harmless.” *Carson Harbor Village, Ltd. v. Unocal Corp.*, No. 96-cv-3281 MMM, 2003 WL 22038700, at *2 (C.D. Cal. Aug. 8, 2003). The party facing the sanction carries the burden of demonstrating that the failure to comply with rules concerning expert testimony is substantially justified or harmless. *Torres v. City of Los*

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Angeles, 548 F.3d 1197, 1213 (9th Cir. 2008); *see also Yeti by Molly*, 259 F.3d at 1107 (“Implicit in Rule 37(c)(1) is that the burden is on the party facing sanctions to prove harmlessness.”).

The May 4 and May 25 Declarations contain new opinions that contradict Dr. Williams’ expert disclosures and deposition testimony. The May 4 Declaration shifted Dr. Williams’ definition of “melting point” upon which each of his earlier opinions were based and provided a much deeper analysis with respect to the significance of FIG. 4 in light of this new construction. The May 25 Declaration goes even further, relying on documents Dr. Williams admitted he had not reviewed as late as his deposition and for the first time purporting to predict the eutectic nature of the Accused Supplements in light of all their ingredients. *See Williams May 25 Decl.* ¶ 8. The May 25 Declaration also opines on a new theory of infringement whereby each of the Accused Supplements is purportedly produced by first creating a binary mixture of CoQ10 and d-limonene, allowing Dr. Williams to conclude that the melting point of the CoQ10 has been reduced based on FIG. 4, and to which the other ingredients are then added. *Id.* ¶ 10. He then dedicates several pages to previously undisclosed opinions regarding why the addition of these ingredients does not affect the eutectic nature of the Accused Supplements. *Id.* ¶¶ 11-13.

JFI has offered no “substantial justification” for its dilatory conduct. Defendant’s claim construction and noninfringement arguments with respect to the melting point reduction limitation have been clear since at least June 2011. *See Sankaran Decl.*, Ex. 19 (Soft Gel’s response to Interrogatory No. 5 which explicitly notes that “Jarrow has provided no evidence that Soft Gel’s accused products are a eutectic based delivery system, that D-limonene melts or lowers the melting point of CoQ10, or that the D-limonene and CoQ10 form a eutectic mixture or a eutectic reaction, and there is evidence to the contrary, namely [Palamakula.] As such, Soft Gel denies Jarrow’s assertions that the accused products are a eutectic based delivery system, that D-limonene melts or lowers the melting point of CoQ10, or that D-limonene and CoQ10 form a eutectic mixture or eutectic reaction.”). Further, the belated disclosures are not harmless. By waiting until the last day to file motion and then filing a supplemental expert declaration in connection with its cross-motion for summary judgment, JFI necessarily deprived Defendants of the opportunity to tailor their summary judgment positions on claim construction, infringement, and invalidity to address Plaintiff’s expert opinions. The May 25 Declaration is even more egregious.

In view of the automatic nature of the exclusionary sanction, the Ninth Circuit “give[s] particularly wide latitude to the district court’s discretion to issue sanctions under Rule 37(c)(1).” *Yeti by Molly*, 259 F.3d at 1106. For example, the Ninth Circuit has affirmed the exclusion of untimely expert testimony where the plaintiff unjustifiably missed the deadline for

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disclosing expert witnesses by twenty days and missed the deadline for submitting expert reports by six weeks. *Quevedo v. Trans-Pacific Shipping, Inc.*, 143 F.3d 1255, 1258 (9th Cir. 1998) (upholding exclusion of untimely expert testimony submitted by plaintiff in opposition to summary judgment); *accord O2 Micro Intern. Ltd. v. Monolithic Power Systems, Inc.*, 467 F.3d 1355, 1368 (Fed. Cir. 2006) (upholding district court's rejection of supplemental expert report and supplemental expert declarations filed in response to summary judgment because proffering party had offered no explanation for why the amended infringement contentions had not been included in the original expert report). Plaintiff's conduct is the very definition of sandbagging, and the May 4 and May 25 Declarations are hereby EXCLUDED. *See Plumley*, 2010 WL 8160423, at *4.

Defendants also object to the declaration of Dr. Nazzal, filed on May 4. Dr. Nazzal was not identified as an expert and no written expert reports of any kind were provided disclosing the basis for his opinions. JFI contends the declaration should not be stricken because, as an inventor, Dr. Nazzal may testify regarding his personal knowledge and is not transformed into an expert simply by virtue of his technical background. *See JFI MSJ Reply*, 7:17-26. JFI’s recitation of the law is correct insofar as it goes, but it does not end the inquiry. *See Baratto v. Brushworks Fine Arts, Inc.*, 701 F. Supp. 2d 1068, 1074 (W.D. Wis. 2010) (noting that the relevant distinction is between expert and lay *testimony*, not expert and lay *witnesses*, and that “testimony is expert in nature when it is the type that could have been offered by any individual with specialized knowledge of the relevant topic.”) (quotations and alterations omitted).

The portions of Dr. Nazzal's declaration pertinent to Plaintiff's infringement contentions are expert opinions that could have been provided by anyone of skill in the art. They are not based on Dr. Nazzal's first-hand experiences conducting the background experiments, for example. Rather, they are largely duplicative of and track Dr. Williams' reports. *See Nazzal Decl.*, ¶ 14 ("lemon oil, which is reported to be 90% d-limonene, reduces the melting temperature of CoQ10 to below about 37 C at a "C:L" ratio (i.e., CoQ10:Lemon oil) of 60:40. Because lemon oil is 90% d-limonene, the observed depression in CoQ10's melting temperature can be attributed to d-limonene"); ¶ 15 ("The '786 patent describes and teaches that mixing CoQ10 with a suitable amount of a volatile essential oil would melt the CoQ10 according to FIG. 4, which could then be mixed with additional ingredients using routine experimentation and optimization such that the solubility of the CoQ10 in the entire multi-component system can be maintained at a desired temperature."). Moreover, the Nazzal Declaration discloses that Dr. Nazzal has been "retained as a consultant" in this case, and that he is being compensated at a rate of \$300 an hour. Accordingly, all expert testimony proffered by Dr. Nazzal is hereby STRICKEN as untimely.

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2. Conclusion regarding infringement

As the party bearing the burden of proof on infringement, Plaintiff was required to come forward with affirmative, admissible evidence sufficient to establish a genuine dispute of fact with respect to every claim limitation. *See Celotex*, 477 U.S. at 322-23. For the reasons set forth above, the admissible evidence adduced by Plaintiff prior to May 4 provides no basis from which a jury could conclude that the CoQ10 in the Accused Supplements is liquid at or below 37 C due to a change in its physical properties, i.e., a reduction in its melting point. *See Anderson*, 477 U.S. at 250-51. Moreover, JFI does not contend that the doctrine of equivalents applies in the event the Accused Supplements simply dissolve ubiquinone.⁷ Accordingly, summary judgment is GRANTED as to Soft Gel and NOW on all claims. *See O2 Micro*, 467 F.3d at 1369 (summary judgment proper where, following the district court's order striking untimely expert reports, the plaintiff had "failed to timely provide evidence in support of" its infringement contentions).

B. Invalidity

In the alternative, were the Court to adopt either of Plaintiff's constructions and hold the melting point reduction limitation is satisfied anytime ubiquinone dissolves or "is liquid" in essential oil at or below 37 C, the Court agrees that the '786 patent is invalid. By direction of 335 U.S.C. § 282, an issued patent is presumed valid. Invalidity must be proven by clear and convincing evidence. *See Microsoft Corp. v. i4i Ltd. Partnership*, — U.S. —, 131 S. Ct. 2238, 2242 (2011). Anticipation requires that the elements of the claims be described in a single prior art reference, either explicitly or inherently. Section 103(a) governs obviousness, and "forbids issuance of a patent when 'the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter

⁷For infringement under the doctrine of equivalents to apply, "the differences between the claimed device and the accused device must be insubstantial." *Zygo Corp. v. Wyko Corp.*, 79 F.3d 1563, 1570 (Fed. Cir. 1996). Soft Gel points out that it was recently awarded a patent covering "to the surprising discovery" that ubiquinone "readily dissolves" in monoterpenes, such as limonenes and derivatives. *See Dash Decl.*, Ex. 7, 1:66-2:1. This patent issued over the '786 patent and "is thus presumed nonobvious in view of the ['786] patent until proven otherwise." *Zygo*, 79 F.3d at 1570 ("The nonobviousness of the accused device, evidenced by the grant of a United States patent, is relevant to the issue of whether the change therein is substantial."); *accord National Presto Indus., Inc. v. West Band Co.*, 76 F.3d 1185, 1192 (Fed. Cir. 1996) ("The fact of separate patentability is relevant, and is entitled to due weight.").

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pertains.”” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The framework for applying the statutory language of § 103(a) is as follows:

Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unresolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented.

Graham v. John Deere Co. of Kansas City, 383 U.S. 1, 17-18 (1966); *KSR*, 550 U.S. at 407 (noting that while the sequence of these question might be recorded in any particular case, the factors continue to define the controlling inquiry).

Under JFI’s original construction that eutectic and melting point all mean dissolve or solubilize, the independent claims boil down to a composition of ubiquinone dissolved in essential oil at 37 C or below. *See SG MSJ*, 17:1-3. Likewise, a disclosure indicating that ubiquinone can be dissolved in essential oil at room temperature is all that is required to inherently anticipate JFI’s current construction of the melting point reduction limitation as reducing “the temperature at which CoQ10 is liquid in an essential oil” to 37 C or below. *See Schering Corp. v. Geneva Pharmaceuticals*, 339 F.3d 1373, 1377 (Fed. Cir. 2003) (“a prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference.”). The dependent claims add limitations directed to a surfactant, particular essential oils, and a capsule.

The Motoyama Japanese patent application (“Motoyama”) discloses “an oral ubiquinone formulation...” and explains that “[t]he inventors of the present invention discovered that ubiquinone was particularly soluble in carvone, which is a liquid at room temperature.” *See Dash Decl.*, Ex. 10 at SGT 12, Column 2; SGT 13, Column 1. Motoyama explains that ubiquinone is added to an oil and stirred. *Id.* at SGT 15, Column 2. If the oil is a liquid at room temperature, like carvone, no heating is required. *See id.* The mixture is then encapsulated in a soft capsule. *See id.* Motoyama discloses that “carvone is a particularly preferred oil due to good solubility for ubiquinone and the property of dissolving an equal weight of ubiquinone at room temperature.” *Id.*, SGT 16, Column 2. “Carvone is present as l-carvone in spearmint oil and peppermint oil.” *Id.* Dr. Williams agrees that Motoyama discloses that l-carvone, which is an essential oil, dissolves ubiquinone at room temperature. *See Dash Decl.*, Ex. 21 (Williams Depo. 57:12-58:25; 93:1-24). By necessity, Motoyama therefore also discloses that ubiquinone

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“is liquid” in l-carvone, an essential oil, at room temperature. *See Schering*, 339 F.3d at 1377. Room temperature is about 25 C, which is less than 37 C. *Dash Decl.*, Ex. 2 ¶ 16. Motoyama also discloses the use of a soft capsule, and “recourse to common sense” dictates that the substitution of either a hard or a soft capsule would be obvious to a PhD-level pharmaceutical researcher. *See KSR*, 550 U.S. at 421; *Dash Decl.*, Ex. 10 at SGT 15, Column 2. Therefore, Motoyama anticipates or renders obvious Claims 1, 4, and 8-13.⁸

Motoyama also anticipates Claim 2, which adds the limitation that “said volatile essential oil is selected from the group consisting of menthol, spearmint oil, peppermint oil, lemon oil, anise, oil, and mixtures thereof.” Motoyama meets this limitation, disclosing that peppermint oil and spearmint oil “readily dissolve ubiquinone and thus are preferred as dispersion media.” *See Dash Decl.*, Ex. 10 at SGT 12, Column 2.

Claim 3 provides “[t]he orally administered dietary supplement of claim 1, further comprising a surfactant.” While Motoyama does not disclose the use of a surfactant, Anderson, another prior art reference describing the use of “essential oils of ginger and sweet basil [] to solubilize the bioactive compound ubiquinone (a coenzyme Q10)” does, and it is undisputed that the use of surfactants in the delivery of drugs or nutritional supplements is well known to one of ordinary skill, which in this case means a PhD-level pharmaceutical researcher. Both Plaintiff’s and Defendants’ experts agree. *See Dash Decl.*, Ex. 2, p. 15 (Dash January 20 Report); *Sankaran Decl.*, Ex. 21 (Williams Depo. 103:20-105:19) (“But the bottom line is, it would be their choice.”). A third prior art reference, Nutramax, which describes a ubiquinone dietary supplement that is “[s]tabilized by Nutramax Laboratories exclusive Antioxidant Protection System using a blend of Rosemary and Sage extracts plus essential oils from spices,” also discloses the use of a surfactant. *See Sankaran Decl.*, Ex. 21 (Williams Depo. 108:25-109:4) (“Well, I think one of ordinary skill in the art reading the fact that they’re emulsified would indicate that...its going to have a surfactant.”).

Accordingly, the addition of a surfactant is but a slight difference and Claim 3 is obvious in light of Motoyama, Anderson, and Nutramax. *See KSR*, 550 U.S. at 412, 422-23 (approving district court’s finding of obviousness based on determination of level of ordinary skill, evaluation of prior art, and finding of “little difference” between the teachings of the prior art and the claims at issue. Specifically, “Asano taught everything contained in claim 4 except the use of a sensor to detect the pedal’s position and transmit it to the computer controlling the

⁸Claims 4, 5, and 9 also require the use of a surfactant. Although Motoyama does not disclose a surfactant, for the reasons discussed in connection with Claim 3, the use of a surfactant would be obvious to one of ordinary skill.

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throttle. That additional aspect was revealed in sources such as the '068 patent and the sensors used by Chevrolet.”). And because Claim 5 is simply a combination of Claims 2 and 4, it, too, is obvious.

Claim 6 provides “[t]he eutectic-based delivery system of claim 5, wherein said essential oil is lemon oil.” Motoyama teaches that peppermint oil and spearmint oil “readily dissolve ubiquinone and thus are preferred as dispersion media.” Anderson and Nutramax use other essential oils, but none specifically recites lemon oil. However, U.S. Patent No. 6,207,137 (“Shuch”) states that “[e]ssential oils such as lemon and tangerine oil may be use[d] as solubilizers for the non-water soluble components of the active ingredient blend.” The active ingredient blend contains ubiquinol. Shuch also discloses that the formulation described may be used as “nutritional supplements either for topical application or ingestion.” *See Dash Decl.*, Ex. 2, p. 13. Dr. Dash opines that Shuch may be combined with Motoyama and/or Anderson, and that the suggestion to combine comes from the fact that Motoyama, Anderson and Shuch, like the '786 patent, all target the same problem of ubiquinone insolubility. *See id.* As in *KSR*, “a person having ordinary skill in the art could have combined [Motoyama, Anderson, and/or Nutramax] with [a different essential oil, such as lemon oil] in a fashion encompassed by [Shuch,] and would have seen the benefits of doing so.” 550 U.S. at 422, 424 (concluding that the “proper question to have asked was whether a pedal designer of ordinary skill, facing the wide range of needs created by developments in the field of endeavor, would have seen a benefit to upgrading Asano with a sensor.”).

Dr. Dash opines that, in light of the common and well-known problem of ubiquinone’s poor solubility, combined with the disclosures that a variety of essential oils solubilize CoQ10, the “substitution of lemon oil for other essential oils is a predictable variation that would be known to one of ordinary skill,” and that it would, “at a minimum, be obvious to use or obvious to try lemon oil based on the teaching of the Shuch patent, or the level of ordinary skill in the art and the knowledge [of] a person of ordinary skill regarding the wide range of essential oils available.” *Id.*, p. 14; *KSR*, 550 U.S. at 419-20, 421. Moreover, while Shuch was before the PTO, Motoyama, Anderson, and Nutramax were not. *See KSR*, 550 U.S. at 426 (declining to reach the question whether the failure to disclose relevant prior art during prosecution voided the presumption of validity given to issued patents, but nevertheless finding “it appropriate to note that the rationale underlying the presumption—that the PTO, in its expertise, has approved the claim—seems much diminished here.”).

In sum, the vast majority of the claims are anticipated by Motoyama. And while JFI argues that Motoyama “fails to present any data” to support the disclosure that carvone dissolves an equal weight of ubiquinone at room temperature, JFI presents no authority that further “data”

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is required beyond the disclosure itself, particularly where it is so simple and straightforward. “Anticipation does not require the actual creation or reduction to practice of the prior art subject matter; [it] requires only an enabling disclosure.” *Schering*, 339 F.3d at 1380. To enable, Motoyama need only “describe how to make” the ubiquinone:l-carvone solution at room temperature, *i.e.*, by combining them at equal weights and stirring, which it does. *See id.* at 1380-81. One of skill in the art could practice its teachings without undue experimentation; accordingly, Motoyama provides an enabling disclosure for dissolving or reducing the temperature at which ubiquinone is liquid in an essential oil to 37 C or below. Those claim limitations not directly encompassed by Motoyama are slight and obvious in light of at least Anderson, Nutramax and Shuch. Based on the content of the prior art, the limited scope of the claims under the construction analyzed, and the high level of ordinary skill, Defendants have shown by clear and convincing evidence that each of the ‘786 patent’s claims are anticipated or obvious.

C. Summary Judgment Conclusion

Based on the foregoing discussion, the Court GRANTS Defendants’ motion for summary judgment of noninfringement based on the construction set forth above. In the alternative, were the Court to accept either of Plaintiff’s disclosed constructions, the ‘786 patent is invalid as anticipated and/or obvious.

V. Conclusion

In sum, the Court construes the preamble as non-limiting, “melting point” to mean “the temperature at which a chemical agent has a transition from solid to liquid due to the application of heat” and “reduc[tion of] the melting point” to require “a change or modification of the physical properties of ubiquinone; *i.e.*, depression of its melting point,” and not merely dissolution. The Court STRIKES the May 4 and May 25 Williams Declarations as untimely and improper supplemental reports, and STRIKES the portion of Dr. Sami Nazzal’s declaration that offers expert, as opposed to lay testimony. In light of the Court’s claim construction and evidentiary rulings, Plaintiff has failed to raise a triable issue of fact that the Accused Supplements meet the melting point reduction limitation shared by all claims. Accordingly, Defendants’ motion for summary judgment based on noninfringement is GRANTED. Further, were the Court to accept Plaintiff’s proposed construction and construe the melting point reduction limitation as satisfied whenever CoQ10 *is liquid* in essential oil at or below 37 C, the Court would grant Defendants’ motion on the alternative grounds that each of the claims disclosed in the ‘786 patent is invalid as anticipated or obvious.

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IT IS SO ORDERED.

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Present:	The Honorable Philip S. Gutierrez, United States District Judge
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Wendy Hernandez	Not Reported
Deputy Clerk	Court Reporter / Recorder

Attorneys Present for Plaintiff(s):

Attorneys Present for Defendant(s):

Thomas Rechen
Mark D. GiarratanaSri Sankaran
Devan V. Padmanabhan**Proceedings: (In Chambers): Findings of Fact and Conclusions of Law
Following Bench Trial**

A bench trial was held in this matter on June 13, 2013. After considering the evidence offered at trial and the arguments of the parties, the Court finds that Soft Gel Technologies, Inc. has failed to establish by clear and convincing evidence that Jarrow Formulas, Inc., in conjunction with the Office of Technology Transfer & Intellectual Property at Texas Tech University, misrepresented or omitted material facts with the specific intent to deceive the Patent and Trademark Office in its Declaration in support of its Petition to Revive U.S. Patent No. 7,588,786, which was deemed abandoned on August 25, 2005.

I. Background & Procedural History

The present matter relates to a dispute between Soft Gel Technologies, Inc. ("Soft Gel") and Jarrow Formulas, Inc. ("JFI") regarding a patent for an orally-administered dietary supplement, U.S. Patent No. 7,588,786 ("the '786 patent"). JFI is a manufacturer of nutritional supplements and the holder of the '786 patent. Soft Gel also manufactures nutritional supplements, including supplements that JFI claimed infringe on the '786 patent ("Accused Supplements"). On November 2, 2010, JFI filed suit against one of Soft Gel's customers, Defendant NOW Health Group, Inc. d/b/a NOW Foods ("NOW"), alleging that NOW had infringed the '786 patent by offering the Accused Supplements for sale. Soft Gel filed a related action against JFI seeking declarations of patent noninfringement, invalidity, and unenforceability due to inequitable conduct. Dkt. # 53; *Soft Gel Tech., Inc. v. Jarrow Formulas, Inc.*, CV 11-0164 PSG (JCx), Docket No. 1 (Jan. 6, 2011). JFI answered and counterclaimed against Soft Gel for infringement and willful infringement. *See id.*, Docket No. 14 (Feb. 2, 2011). The Court consolidated the two cases. *See id.*, Docket No. 39 (May 2, 2011).

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Both parties moved for summary judgment. *See* Dkts. # 98, 100. Soft Gel moved for summary judgment on noninfringement and invalidity while JFI moved for summary judgment on infringement, validity, and no inequitable conduct. *Id.* On August 2, 2012, the Court granted summary judgment in favor of Defendants, finding that there was no infringement and that the ‘786 patent was invalid as anticipated and/or obvious. *See* Dkt. # 156. The Court did not address the inequitable conduct claim, which is now the only issue remaining before the Court. *See id.*

II. Findings of Fact

On November 14, 2001, George M. Cooper of the law firm Jones, Tullar & Cooper filed a provisional patent application titled “Eutectic-Based Self-Nanoemulsified Drug Delivery System” (“‘786 patent application”) with the Patent and Trademark Office (“PTO”) on behalf of H. Walter Haeussler (“Haeussler”), Director of the Office of Technology Transfer & Intellectual Property at Texas Tech University (“Texas Tech”). *Ex. 504.* A year later, on November 14, 2002, Texas Tech filed a utility patent application claiming priority to the provisional patent application, Application Serial No. 10/293,932, which issued on September 15, 2009 as U.S. Patent No. 7,588,786, the ‘786 patent. *Ex. 504.* The ‘786 patent application was prosecuted by Texas Tech from late 2001 until mid-2005 and was officially deemed abandoned by the PTO on or about August 25, 2005. *Ex. 544.*

Lance Anderson (“Anderson”) replaced Haeussler as the Director of the Texas Tech Technology Transfer & Intellectual Property Office in or about August 2004 and oversaw the prosecution of the ‘786 patent application with the assistance of outside counsel Jennifer Yancy (“Yancy”) and the ‘786 patent’s co-inventors, Dr. Mansoor Khan (“Dr. Khan”) and Sami Nazzal (“Nazzal”). *Ex. 554: Anderson Decl. ¶ 2.* On February 13, 2003, Texas Tech filed a Preliminary Amendment to the ‘786 patent application with comments by Dr. Khan and Nazzal. *Ex. 564: Anderson Dep. 68:8-18; Ex. 513.* On or about October 16, 2003, the Examiner for the PTO subjected the claims of the ‘786 patent application to a restriction requirement requiring an election between the claims. *Ex. 516.* Anderson sent a fax to Dr. Khan on October 22, 2003, asking to discuss the restriction requirement. *Ex. 564: Anderson Dep. 68:8-18; Ex. 517.* On October 23, 2003, Anderson sent a fax to Yancy ordering her to “proceed as you recommend.” *Ex. 518.* The PTO mailed a first Office Action regarding the ‘786 patent application on November 28, 2003. *Ex. 519.* On February 27, 2004, Texas Tech filed a response to the Office Action. *Ex. 520.* On May 19, 2004, the PTO mailed a second Office Action regarding the ‘786 patent application. *Ex. 524.*

In June 2004, Dr. Kahn resigned from Texas Tech and took a position with the Food and Drug Administration (“FDA”). *Ex. 564: Anderson Dep. 81:11-13; 84:20-85:5.* For a period of

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time after Dr. Khan joined the FDA, Texas Tech continued to actively prosecute the '786 patent application with Dr. Kahn's assistance. *Ex. 564: Anderson Dep.* 81:11-83:5; 83: 20-23; 84: 20-88:4. On July 27, 2004, Anderson e-mailed Dr. Khan requesting his assistance in responding to the May 19, 2004 Office Action. Dr. Khan responded "I will be happy to assist you all to complete what we started before I joined the FDA." *Ex. 525.* On August 13, 2004, Dr. Khan e-mailed comments regarding the Office Action to Anderson and Yancy. *Ex. 528.* Yancy interviewed with a PTO Examiner to discuss the inventor's comments on October 19, 2004. *Ex. 529.* Yancy also filed a response to the May 19, 2004 Office Action following the interview with the Examiner. *Ex. 530.*

On January 13, 2005, the PTO mailed a third Office Action regarding the '786 patent application. *Ex. 531.* The January 13, 2005 Office Action required a response within three months, ending on April 13, 2005. *Ex. 531.* The PTO, through the January 13 Office Action, rejected the claims on multiple grounds, including 35 U.S.C. §§ 112 & 102 (anticipation) and 35 U.S.C. § 103 (obviousness). On January 21, 2005, in a letter to Anderson regarding the PTO's rejection of the '786 patent application, Yancy stated that "[w]e can respond to this rejection by amending the claims to recite the three drugs listed by the Examiner (i.e. ubiquinone, cyclosporine, and Vitamin E)," but noted that doing so would "limit the breadth of the protection for the invention." *Id.* Yancy also stated "it appears that amending the claims to include the three listed drugs would overcome the [§ 102] rejection." *Id.* However, Yancy did not indicate any possible response to the § 103 rejection on the basis of obviousness.

On February 16, 2005, Anderson e-mailed Dr. Khan regarding the status of his pending patent applications, but Dr. Khan did not respond. *Ex. 533.* Yancy then sent a reminder about the Office Action deadline to Texas Tech and Anderson on March 2, 2005. *Ex. 532.* On March 8, 2005, Anderson sent Dr. Khan another e-mail, stating "I have yet to hear back from you. ... We are planning to abandon our applications that involve you." *Ex. 533.* In his deposition, Anderson testified that he told Dr. Khan that Texas Tech would abandon the patent in order to motivate Dr. Kahn to respond and assist in prosecuting the '786 patent application. *Ex. 564: Anderson Dep.* 113:23-114:8. Dr. Kahn responded to this e-mail from Anderson on the same day, offering support to Texas Tech in prosecuting the '786 patent application. *Id.* Dr. Khan stated that he would "be happy to provide all the information that you need... [and] the data that was required." *Id.*

No emails or faxes were exchanged between Anderson and Dr. Khan following this March 8 email until Anderson sent a fax to Dr. Khan on June 1, 2005, stating that Texas Tech "would like to offer to release the rights of this patent application, or discuss alternatives with you, so that Texas Tech University is no longer obligated for these expenses." *Ex. 539 at TTU-205.* However, Anderson noted that he made several calls to Dr. Khan in the time between the

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March 8, 2005 e-mail and the June 1, 2005 fax. *Ex.* 572 at ME-12. Yancy reminded Anderson about the pending Office Action deadline in a letter sent on March 25, 2005. *Ex.* 534. Yancy reminded Anderson about the pending deadline for a third time on April 7, 2005, but also noted that the deadline could be extended by a month. *Ex.* 535. On April 26, 2005, Yancy communicated to Anderson that the deadline to respond to the pending Office Action was May 13, 2005, as the first month extension had already taken effect. *Ex.* 537. Yancy also communicated to Anderson that she was unsure whether the pending Office Action had been forwarded to Dr. Khan. *Id.* On May 3, 2005, Yancy reminded Anderson that the response to the PTO Office Action needed to be filed by May 13, 2005. *Ex.* 538. The May 13 reminder also included a handwritten notation saying “[p]lease extend one month,” which was originally written in a fax from Anderson to Yancy dated May 5, 2005. *Exs.* 538 & 539. Yancy then informed Anderson that the second month extension had begun and that the pending Office Action needed to be answered by June 13, 2005. *Ex.* 539. A week later on June 8, 2005, Yancy faxed a reminder to Anderson that a response to the pending Office Action was due by June 13, 2005. *Ex.* 540. Like the earlier reminder, the June 8 reminder included a handwritten note from Anderson that stated “[e]xtend final month.” *Id.* On June 30, 2005, Yancy communicated to Anderson that the final deadline to respond to the pending Office Action was July 13, 2005. *Ex.* 541.

On July 8, 2005, Anderson directed Yancy to let the ‘786 patent application “go abandoned unless you hear otherwise from Dr. Khan.” *Ex.* 542 TTU-200. Anderson communicated to Dr. Khan that Texas Tech was choosing to allow the ‘786 patent application to go abandoned that same day. *Ex.* 543. The ‘786 patent application was officially deemed abandoned by the PTO on August 25, 2005 for failure to “file a proper reply to the Office letter mailed on 13 January 2005.” *Ex.* 544.

On December 21, 2005, Anderson e-mailed Dr. Khan to inform him that JFI, a commercial interest, wanted to revive and purchase the ‘786 patent. *Ex.* 546. In this e-mail, Anderson asked Dr. Khan if he would support this revival attempt, to which Dr. Khan responded “yes.” *Id.* Also on December 21, 2005, Anderson sent a letter to Mark Giarratana (“Giarratana”), counsel for JFI, with a signed agreement between Texas Tech and JFI. *Ex.* 547. The agreement included an exclusive option for JFI to acquire the rights to the ‘786 patent from Texas Tech for \$13,000, if it could be successfully revived, and a \$12,000 payment to execute the option. *Id.* On December 23, 2005, JFI delivered a check to Texas Tech for \$13,000 for the exclusive option to acquire the rights to the ‘786 patent. *Ex.* 548. After receiving \$13,000 from JFI, Anderson and Giarratana began the process to revive the ‘786 patent application. *Exs.* 549-551.

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Anderson, with help from Giarratana, supported the petition to revive the '786 patent application with a Declaration (the "Declaration" or the "Anderson Declaration"), explaining why Texas Tech University had unintentionally abandoned the '786 patent application. *Id.*; *Giarratana Test.* 11:6-8, 48:24- 49:13. The Declaration stated that "it is the policy of Texas Tech to have the faculty inventors participate and provide technical assistance to the Tech Transfer Office and Texas Tech throughout the prosecution of their patent applications." *Ex.* 554: *Anderson Decl.* ¶ 2. The Declaration asserted that Dr. Khan left Texas Tech in January 2005 to take a position with the FDA. *Id.* ¶ 6. In addition, the Declaration stated that Anderson and Texas Tech's attorneys made repeated attempts to "contact Dr. Khan," but were "unable to obtain Dr. Khan's assistance in connection with further prosecution of the Khan patent application." *Id.* ¶ 7. Anderson also stated in the Declaration that he "attempted to notify Dr. Khan that a response was required and his input was necessary, however, despite attempts by e-mail, fax and telephone, I [Anderson] was unable to procure [Dr. Khan's] assistance." *Id.* ¶ 9. Furthermore, the Declaration asserted that "[a]s the six month deadline for responding to the outstanding Office Action approached, I [Anderson] had not received the required assistance from Dr. Khan, and therefore was unable to respond to the outstanding office action prior to the deadline." *Id.* ¶ 10. Anderson then stated in the Declaration that Texas Tech "became aware of a party with expertise who could assist in the prosecution" so Texas Tech has "diligently proceeded to revive the Khan patent application." *Id.* ¶ 11. The "party with expertise" was JFI. At trial, Giarratana testified that all of the statements in the Declaration are true and that he would not change the contents of the Declaration. *Giarratana Test.* 11:18-23. Giarratana's assertion regarding the accuracy of the Declaration, however, is partially contradicted by Anderson, who testified in his deposition that "as I read it [the Declaration] today, under the—the level of scrutiny, there may be issues that aren't completely—completely correct. But yes, otherwise, it's—it's accurate and truthful."

On January 27, 2006, Anderson faxed a signed copy of the Anderson Declaration to Giarratana. *Ex.* 553. On February 1, 2006, the Petition to Revive was delivered to and received by the PTO with the Anderson Declaration attached. *Ex.* 554: *Anderson Dep.* 174:22-25. On June 2, 2006, the PTO granted the petition to revive. *Ex.* 555. On July 18, 2006, Anderson e-mailed Giarratana asking if JFI would exercise its exclusive option to purchase the '786 patent. *Ex.* 557. Giarratana responded by stating that JFI "would like to exercise the option and complete the purchase of the patent application." *Id.*

III. Conclusions of Law

A. Legal Standard

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Under *Therasense, Inc. v. Becton, Dickinson and Co.*, to prevail on a claim of inequitable conduct, a party must prove that the applicant misrepresented or omitted material information in the patent application with the specific intent to deceive the PTO. 649 F.3d 1276, 1287 (Fed. Cir. 2011) (en banc). The party must prove both elements—intent and materiality—by clear and convincing evidence. *Id.*

Regarding materiality, the Federal Circuit determined that “the materiality required to establish inequitable conduct is but-for materiality.” *Therasense*, 649 F.3d at 1291. In a case based on failure to disclose information to the PTO, the omission is but-for material if the PTO would not have allowed a claim had it been aware of the omitted information. *Id.*; see also *Novo Nordisk A/S v. Caraco Pharm. Lab., Ltd.*, 719 F.3d 1346, 1358-59 (Fed. Cir. 2013) (finding that the omission of information that “ideally would have been disclosed to the PTO” was not material under the *Therasense* standard because its disclosure would not have affected the ultimate conclusion of the PTO). Thus, in assessing the materiality of omitted information, the court must determine whether the PTO would have allowed the claim if it had been aware of the undisclosed information. *Therasense*, 649 F.3d at 1291.

However, the court in *Therasense* also created an exception for proving but-for materiality that applies “[w]hen the patentee has engaged in affirmative acts of egregious misconduct, such as the filing of an unmistakably false affidavit.” *Id.* In such cases, the prior art is material, even absent a showing of clear and convincing evidence that the PTO would not have allowed the claim if it had been aware of the prior art or undisclosed information. *Id.* at 1292; see also *Rohm & Haas Co. v. Crystal Chem. Co.*, 722 F.2d 1556, 1570-71 (Fed. Cir. 1983). The exception means that “for deliberately planned and carefully executed schemes, materiality will be assumed.” See *Network Signatures v. State Farm Mutual Auto. Ins. Co.*, No. SACV 11-00982 JVS (RNBx), 2012 WL 2357307, at *7 (C.D. Cal. June 13, 2012). The standard for proving egregious misconduct such that but-for materiality is presumed is high: The *Therasense* court specified that “neither mere nondisclosure of prior art references to the PTO nor failure to mention prior art references in an affidavit constitutes affirmative egregious misconduct.” *Therasense*, 649 F.3d at 1292-93. Therefore, claims of inequitable conduct that are based on such omissions require proof of but-for materiality. *Id.*

In order to prove intent in a case based on nondisclosure of information to the PTO in a patent application, “clear and convincing evidence must show that the applicant *made a deliberate decision* to withhold a *known* material reference.” *Therasense*, 649 F.3d at 1290 (quoting *Molins PLC v. Textron, Inc.*, 48 F.3d 1172, 1181 (Fed. Cir. 1995)). To meet the clear and convincing evidence standard in this context, “the specific intent to deceive must be ‘the single most reasonable inference able to be drawn from the evidence.’” *Id.* (quoting *Star Scientific, Inc. v. R.J. Reynolds Tobacco Co.*, 537 F.3d 1357, 1366 (Fed. Cir. 2008)). Therefore,

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“when there are multiple reasonable inferences that may be drawn, intent to deceive cannot be found.” *Id.* at 1290-91; *see also Scanner Techs. Corp. v. ICOS Vision Sys. Corp.*, 528 F.3d 1365, 1376 (Fed. Cir. 2008). Further, when direct evidence of deceptive intent is not available, “a district court may infer intent from indirect and circumstantial evidence.” *Therasense*, 649 F.3d at 1290; *see also Larson Mfg. Co. of S.D., Inc. v. Aluminart Prods. Ltd.*, 559 F.3d 1317, 1340 (Fed. Cir. 2009). However, in an inequitable conduct claim, a finding of intent may not be based on evidence that the misrepresentation or omission amounted to negligence or gross negligence under a “should have known” standard. *Therasense*, 649 F.3d at 1290; *see also Kingsdown Med. Consultants, Ltd. v. Hollister Inc.*, 863 F.2d 867, 876 (Fed. Cir. 1988)). As such, “[p]roving that the applicant knew of a reference, should have known of its materiality, and decided not to submit it to the PTO does not prove specific intent to deceive.” *Therasense*, 649 F.3d at 1290; *see also Star Scientific*, 537 F.3d at 1366.

B. Discussion

In order to find in Soft Gel's favor and conclude that the '786 patent is unenforceable due to inequitable conduct, the Court must find that Soft Gel has proven by clear and convincing evidence that Texas Tech misrepresented or omitted material facts in the '786 patent and that it did so with the specific intent to deceive the PTO. However, in this case, the Court finds the second inquiry dispositive, as Soft Gel has failed to prove by clear and convincing evidence that Texas Tech intended to deceive the PTO.

Soft Gel argues that the single most reasonable inference to be drawn from the evidence on the record is that Anderson and Giarratana, on behalf of Texas Tech, acted with specific intent to deceive the PTO in their preparation of the Anderson Declaration in support of the Petition to Revive the ‘786 patent application. *Soft Gel Trial Brief* 18: 8-27. The Declaration in support of the Petition to Revive lays out basic facts surrounding the circumstances of the abandonment of the ‘786 patent. In his Declaration, Anderson states that the ‘786 patent application was prosecuted for “a period of nearly three years,” but in January 2005 “Dr. Khan left Texas Tech and moved out of the state to take a position with the Federal Food and Drug Administration.” *Ex. 554: Anderson Decl.* ¶¶ 4-6. Furthermore, in the Declaration, Anderson states that “[a]s the six month deadline for responding to the outstanding office action approached, I had not received the required assistance from Dr. Khan, and therefore was unable to respond to the outstanding office action prior to the deadline.” *Id.* ¶ 10.

Soft Gel contends that these and other statements in the Declaration were false and that Anderson included them in the Declaration with the specific intent to deceive the PTO. Soft Gel asserts that it was false both that Texas Tech needed Dr. Khan's assistance to respond to the Office Action and that Anderson was unable to procure his assistance. Soft Gel asserts that

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Texas Tech did, in fact, have options for responding to the Office Action without Dr. Khan's assistance. *Soft Gel Trial Brief* 5:13-6:27. In his deposition testimony, Anderson acknowledged that Texas Tech could have pursued other avenues to respond to the Office Action, though he also said that these alternatives were not viable under the circumstances. *See Ex. 564: Anderson Dep.* 267:15-269:18. When asked if Texas Tech could have taken alternative approaches to respond to the pending office action without procuring Dr. Khan's assistance, Anderson testified that "we could have done a lot of things... including authorizing Jennifer Yancy to respond as she suggested." *Ex. 564: Anderson Dep.* 267:19-23; *see also Ex. 531*. Anderson then stated that Texas Tech "could have hired an independent consultant. And we could have also obtained an independent third party. We could have gone to colleagues within [Dr. Khan's] former department. We could have, you know, done a lot of things like that." *Id.* 268: 2-13. Anderson also acknowledged that he could have reached out to Dr. Khan's co-inventor Nazzal for assistance. *Id.* 267:24-268:2. Soft Gel contends that despite these alternate avenues that were available, Texas Tech instead made the deliberate decision that it would not respond without Dr. Khan's assistance. *See Soft Gel Post-Trial Brief* 7:14-24. In support of this argument, Soft Gel points to communications in which Anderson wrote that Texas Tech had "placed the ball in the court of Dr. Khan to give us a response" and "if we had gotten a response from Dr. Khan, we would have filed a response." *See id; Ex. 562* at 180:11-20, 242:24-243:2. Soft Gel further supports this argument by pointing to an email in which Anderson instructed Yancy that she should take no action in further pursuit of the '786 patent application after Dr. Khan had become unresponsive and to take no further action unless she heard from Dr. Khan. *Soft Gel Post-Trial Brief* 7:14-24; *Ex. 542; Ex. 564: Anderson Dep.* 139:17-23. Finally, Soft Gel contends that notes that Giarratana made following a conversation with Anderson further demonstrate that Texas Tech could have proceeded without Dr. Khan's assistance. At trial, Giarratana was questioned about notes he made following a conversation with Anderson on or around September 21, 2005, in which Giarratana wrote that Anderson spoke about a conference call in which he discussed "how easily" Texas Tech could have gotten a response and that it had determined it was "not worth it," though Giarratana did not know to which conference call Anderson referred, with whom Anderson had spoken, or what Anderson had meant by "not worth it." *Bench Trial Tr.* 24:24-26:16.

Soft Gel next contends that Anderson’s statement that he could not procure Dr. Khan’s assistance was false. In his Declaration, Anderson said that “repeated attempts were made by myself and Texas Tech’s attorney to contact Dr. Khan. Despite such attempts, I was unable to obtain Dr. Khan’s assistance.” *Ex. 554: Anderson Decl.* ¶ 7; *Soft Gel Trial Brief* 7:1-8:2. Soft Gel argues that this information is false because Anderson had procured Dr. Khan’s assistance by March 8, 2005 when Dr. Khan offered to provide all the information required for prosecuting the ‘786 patent application, *ex. 533*, but that Anderson failed to follow-up on Dr. Khan’s offer of assistance, *Bench Trial Tr.* 99:3-5. Soft Gel argues that instead of accepting Dr. Khan’s offer to assist in the prosecution of the ‘786 patent application, Texas Tech and Anderson stayed silent

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until sending a fax to Dr. Khan on June 1, 2005 stating that Texas Tech “would like to offer to release the rights of this patent application, or discuss alternatives with you, so that Texas Tech University is no longer obligated for these expenses.” *Ex. 539*. In addition, Soft Gel points to a fax sent to Dr. Khan on July 8, 2005 in which Texas Tech disclaimed interest in responding to the Office Action and stated that Texas Tech would “allow it to go abandoned.” *Ex. 543*. In the fax, Anderson also stated: “[b]y this letter we are returning the invention to you and your co-inventor.” *Ex. 543*. Soft Gel urges the Court to conclude based on this evidence that Texas Tech could have procured Dr. Khan’s assistance but intentionally chose not to do so. *Soft Gel Trial Br. 7:1-8:2*.

Soft Gel also contends that Anderson lied when he stated that the ‘786 patent application was unintentionally abandoned because he testified that he did not know whether the delay and abandonment were intentional, and the evidence on the record demonstrates that Texas Tech had intentionally abandoned the application. *Soft Gel Trial Brief 8:3-11:4*. Soft Gel points to several pieces of evidence on the record that it claims demonstrate that Texas Tech intentionally abandoned the ‘786 patent application. First, Soft Gel contends that the communications with Dr. Khan in March, June, and July 2005 disclaiming any intent to respond demonstrate Texas Tech’s intent to abandon the application. *Id. 8:21-9:23*. On March 8, 2005, Anderson stated that “[w]e are planning to abandon our applications that involve you.” *Ex. 533 at TTU-236*. On June 1, 2005, Anderson stated that he “would like to offer to release the rights of this patent application, or discuss alternatives with you [Dr. Khan], so that Texas Tech is no longer obligated for these expenses.” *Ex. 539 at TTU-205*. Lastly, on July 8, 2005, Anderson stated that Texas Tech “is choosing not to proceed with this and will allow it to go abandoned.” *Ex. 543*. At trial, Soft Gel argued that, even if this were a tactic to motivate Dr. Khan, as Anderson testified in his deposition, it worked in March and there was no need to use it again several months later. *Bench Trial Tr. 99:3-19*. Soft Gel further contends that Anderson’s deposition testimony confirms that the July 8, 2005 fax represented Texas Tech’s intention to abandon the patent application. In his deposition, Anderson stated: “I’m taking a pretty concrete approach with this [fax] in order to assure we’re, you know, clear on [the ‘786 patent application] going abandoned.” *Ex. 564: Anderson Dep. 223:23-224:10*. In further support of this contention, Soft Gel points to the portion of Anderson’s deposition testimony in which he said “yes” when asked if as of July 7, 2005, and July 8, 2005 Texas Tech was no longer interested in responding to the Office Action. *Ex. 564: Anderson Dep. 219:10-18; 224:11-14*.

It is Soft Gel’s contention that Anderson falsely represented to the PTO that he could not proceed without Dr. Khan’s assistance, that he could not procure Dr. Khan’s assistance, and that Texas Tech had unintentionally abandoned the patent with the specific intent to deceive the PTO in order to revive the ‘786 patent. *Soft Gel Trial Br. 1:11-15, 2:3-22*. Soft Gel further contends that Anderson and Giarratana believed that the information not disclosed to the PTO was but-for

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material and that the '786 patent application would be revived only by omitting that information. *Id.* 2:13-14. Soft Gel points to several circumstances in support of its contention that Anderson, with Giarratana's assistance, omitted this information with the specific intent to deceive. First, Soft Gel contends that Anderson knew the true circumstances surrounding the abandonment of the '786 patent application and knew that the statements he made in his Declaration were false. *Soft Gel Trial Br.* 9:16-17. From this, Soft Gel contends that the Court can infer that he deliberately provided false information. *Id.* 2:13. Soft Gel further contends that because the truth was the "exact opposite of the central pillar of the Declaration" and "destroy[ed] the factual basis of the Declaration and Petition to Revive," the Court can infer that Anderson deliberately made misstatements that he knew were material. *Soft Gel Post Trial Br.* 5:14-27; 9:23-35. In other words, it is Soft Gel's contention that because Anderson and Giarratana put facts into the declaration that were in "stark contrast" with the truth, the Court can infer that they were aware of the materiality of the withheld facts. *Soft Gel Trial Br.* 2:13-16. Soft Gel also contends that an intent to deceive can be inferred because Anderson was the decision-maker for Texas Tech on the '786 patent application, knew all of the relevant facts, and knew about JFI's commercial interest in the patent. *Id.* 9:16-17, 11:12-23. Soft Gel argues that Anderson's extensive review of the Declaration demonstrates that his preparation of the false Declaration was deliberate, further supporting the inference that he intended to deceive. *Id.* 6:11-19. Based on all these circumstances, Soft Gel contends that the Court may infer that Anderson acted with the specific intent to deceive. However, in order to find a specific intent to deceive, it is insufficient that the specific intent to deceive is a plausible inference; it must be the "single most reasonable inference to be drawn." *Therasense*, 649 F.3d at 1290. The Court cannot say that the specific intent to deceive is the single most reasonable inference to be drawn from the evidence on the record.

The evidence on the record also supports an inference that Giarratana and Anderson believed the information included in the Declaration to be accurate—*i.e.*, that they believed they had needed Dr. Khan's assistance to prosecute the patent, were unable to procure his assistance, and that the abandonment of the patent was unintentional. Under this scenario, Giarratana and Anderson considered the relevant information, concluded that the information omitted was not relevant, and so did not act with the specific intent to deceive. This version of events is supported by several pieces of evidence on the record. As a preliminary matter, there is no evidence on the record, such as emails or contemporaneous statements by Anderson or Giarratana, showing that either of them believed the inclusion of this information would result in a rejection by the PTO. Further, there is no evidence affirmatively showing that either believed the '786 patent application had been intentionally abandoned, and there is evidence supporting the inference that the abandonment was, in fact, unintentional. First, there is evidence that Texas Tech actually needed, or at least believed it needed, Dr. Khan's assistance in order to prosecute the '786 patent. Such an inference is supported by testimony by Anderson and Giarratana, as

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well as by documents contemporaneous to the patent prosecution. For example, Giarratana's notes stated that the '786 patent was a specialty invention, that no one else on staff understood how to prosecute it, and that Texas Tech did not believe it could prosecute the patent without his input. *Giarratana Test.* 47:9-48:10. Further, while there may initially have been other ways to pursue the '786 patent application with Dr. Khan's assistance, there is evidence that Texas Tech did not consider those options to be realistic by the summer of 2005, given that Texas Tech had relied on Dr. Khan's assistance throughout the patent prosecution. *JFI Post Trial Br.* 5:6-19. JFI contends that based on the circumstances of the patent prosecution in the summer of 2005, it was impractical to pursue any other avenue. *Id.* 5:10-19. By this time, for example, Anderson believed that prosecuting the patent with Nazzal "just wasn't an option," given that they had already spent significant time prosecuting the patent with Dr. Khan's assistance. *Ex.* 564: *Anderson Dep.* 289:12. By this time Anderson also believed that Texas Tech could not pursue the patent with an independent contractor or consultant given that the patent had hitherto been a coordinated effort between Texas Tech and Dr. Khan. *Id.* 289:15-23. Anderson testified that Texas Tech did not intend or desire to abandon the patent but did so due to the circumstances that existed at the time. In his deposition, Anderson testified as follows:

The failure to respond was never the intent of Texas Tech University. The failure to respond was not desired by Texas Tech University. Under the circumstances, we had placed the ball in the court of Khan to give us a response. We did not get the response. And, thus, the patent went abandoned. . . . If we had gotten a response from Khan, we would have filed a response.

Id. 180:23-181:3. In short, JFI contends that even if Texas Tech could have adopted a different approach earlier in the application process, by the summer of 2005, Anderson believed that such alternatives were no longer viable.

Evidence of Anderson and Giarratana's conduct throughout the spring and summer of 2005 also supports the inference that Texas Tech intended to pursue the patent application, sought Dr. Khan's assistance in doing so, and believed it actually needed Dr. Khan's assistance to proceed. Specifically, that Anderson made several calls to Dr. Khan following Dr. Khan's March 8 e-mail indicating his willingness to assist and that Texas Tech accepted three consecutive one-month extensions while waiting to hear from Dr. Khan support the inference that Texas Tech believed it could not pursue the action without him. Further, Anderson's emails to Dr. Khan, including those in which he stated that the patent application would go abandoned, support the inference that Anderson was attempting to procure Dr. Khan's assistance. Anderson's explanation that he used the threat of abandonment to motivate Dr. Khan into cooperation when he did not actually intend to abandon the patent at that time is plausible. All these facts would lead to the conclusion that the '786 patent application was not intentionally

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application with the Dr. Khan's assistance, even without any foreseeable commercial benefit, but could not procure Dr. Khan's assistance after he left for the FDA. Here, Texas Tech attempted to procure Dr. Khan's continued assistance to prosecute the '786 patent application. Though Dr. Khan showed an initial willingness to cooperate, he become unresponsive, preventing Texas Tech from prosecuting the patent. That Anderson made follow up phone calls to Dr. Khan after the March 8 e-mail, that Texas Tech extended the Office Action deadline three times, and the plausible scenario in which Anderson used the threat of abandonment to motivate Dr. Khan into cooperating, all support this version of events. As the deadline approached, it became clear that responding to the Office Action was not possible, or at least that Anderson and others believed this to be the case, and that it was not possible for Anderson to have taken any other alternative actions to respond to the Office Action without deviating from Texas Tech's policy, which requires that all patents be prosecuted with the assistance of the faculty inventor. Under this scenario, Anderson believed Texas Tech could not pursue the patent without Dr. Khan's assistance, was unable to procure his assistance, and did not believe the '786 patent application was intentionally abandoned. Accepting this plausible scenario, Anderson and Giarratana did not omit any information from the Declaration with the intent to deceive.

The standard for a finding of intent to deceive requires that the evidence produce a single reasonable inference of specific intent to deceive the PTO. Such a single reasonable inference is not present in this case, as there are two plausible opposing inferences. Therefore, Soft Gel has not proven this element by clear and convincing evidence.

IV. Conclusion

For the foregoing reasons, the Court finds that Plaintiff and Counter-Defendant Soft Gel Technologies, Inc., failed to prove by clear and convincing evidence that Plaintiff and Counterclaim-Defendant Jarrow Formulas, Inc., misrepresented or omitted material information with the specific intent to deceive the Patent and Trademark Office in its Declaration in support of the Petition to Revive U.S Patent No. 7,588,786. Plaintiff and Counterclaim-Defendant JFI is ordered to file a proposed judgment consistent with this Order and with the Court's August 2, 2012 order granting summary judgment. The proposed judgment shall be filed no later than **September 3, 2013.**

IT IS SO ORDERED.



US007588786B2

(12) United States Patent
Khan et al.**(10) Patent No.: US 7,588,786 B2**
(45) Date of Patent: Sep. 15, 2009**(54) EUTECTIC-BASED SELF-NANOEMULSIFIED
DRUG DELIVERY SYSTEM****(75) Inventors: Mansoor A. Khan**, Amarillo, TX (US);
Sami Nazzal, Amarillo, TX (US)**(73) Assignee: Jarrow Formulas, Inc.**, Los Angeles,
CA (US)**(*) Notice:** Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 0 days.**(21) Appl. No.: 10/293,932****(22) Filed: Nov. 14, 2002****(65) Prior Publication Data**

US 2003/0147927 A1 Aug. 7, 2003

Related U.S. Application Data**(60)** Provisional application No. 60/331,292, filed on Nov.
14, 2001.**(51) Int. Cl.****A61K 36/752** (2006.01)**A61K 36/00** (2006.01)**A61K 9/00** (2006.01)**(52) U.S. Cl.** **424/736; 424/725; 424/400****(58) Field of Classification Search** **424/400,**
424/736; 514/11, 458, 633

See application file for complete search history.

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Primary Examiner—Christopher R Tate*Assistant Examiner*—Randall Winston**(74) Attorney, Agent, or Firm**—McCarter & English, LLP**(57) ABSTRACT**

A eutectic-based self-nanoemulsified drug delivery system (SNEDDS) is formulated from polyoxyl 35 castor oil (Cremophor), medium chain mono- and diglycerides (capmul), essential oils, and a pharmacologically effective drug or nutraceutical or dietary supplement. The preferred pharmacologically effective drug is a poorly water soluble drug, such as ubiquinone (CoQ₁₀). The SNEDDS can be further incorporated into a powder to produce a solid dosage form. The solid dosage form contains the SNEDDS, a copolymer of vinylpyrrolidone and vinyl acetate (Kollidon VA 64), maltodextrin, and microcrystalline cellulose (MCC).

13 Claims, 12 Drawing Sheets

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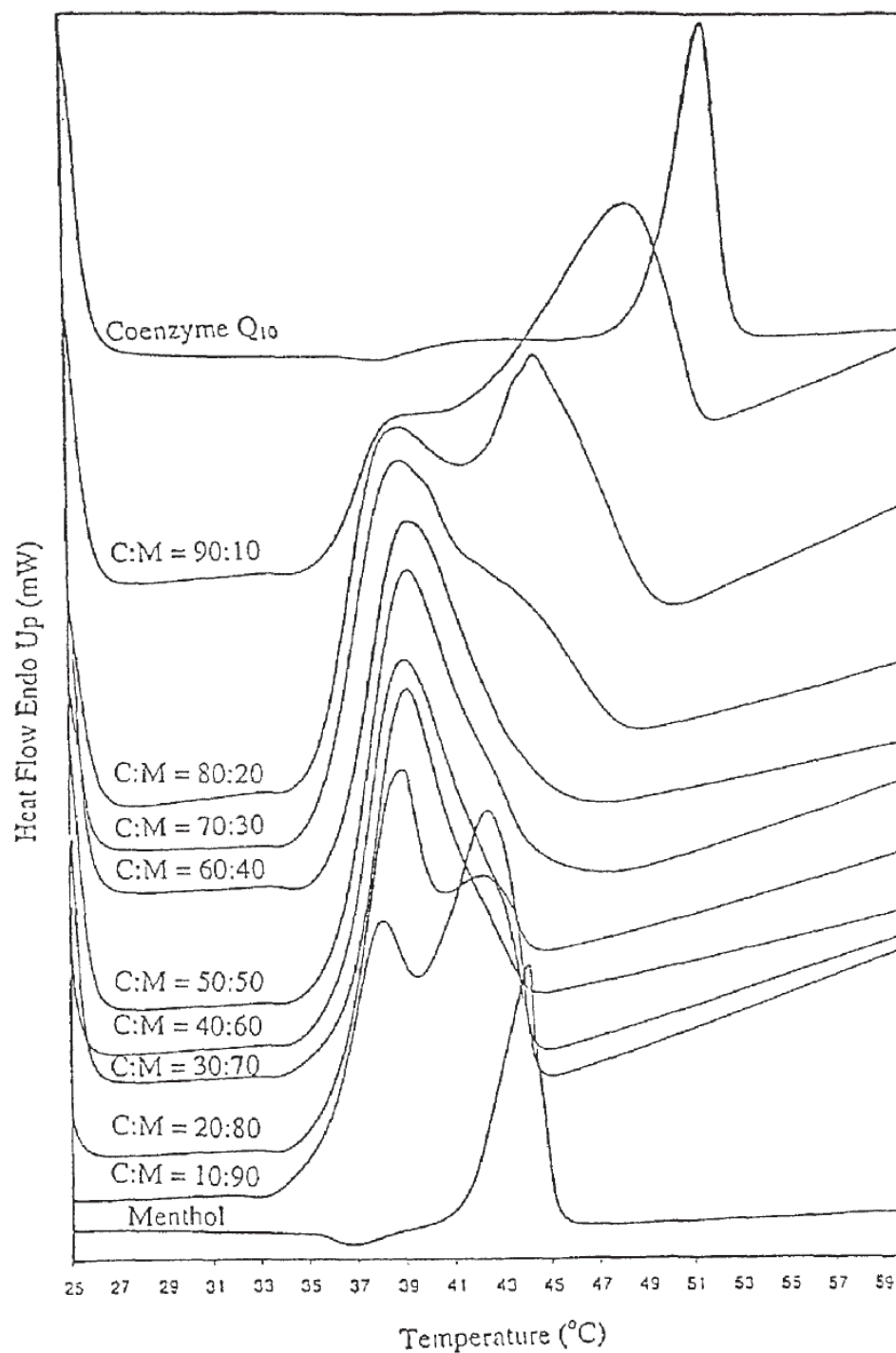


FIG. 1

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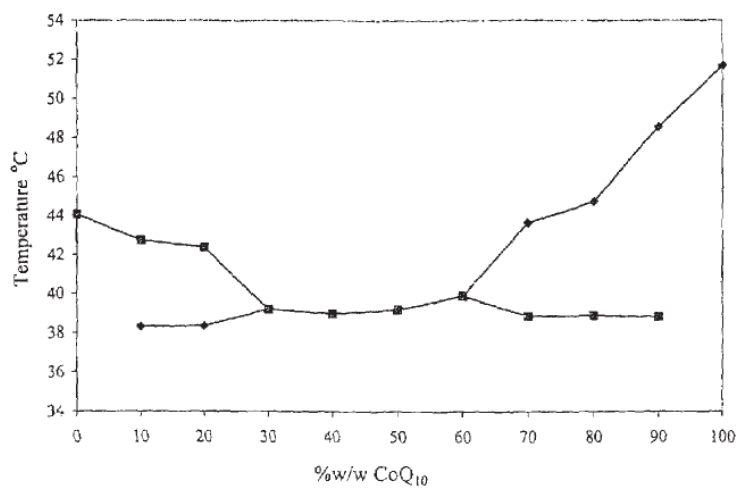


FIG. 2

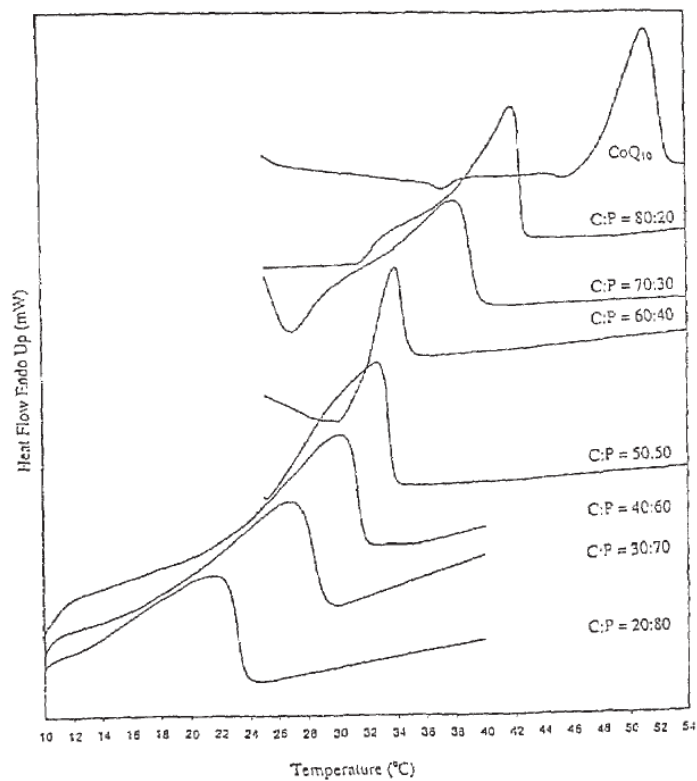


FIG. 3

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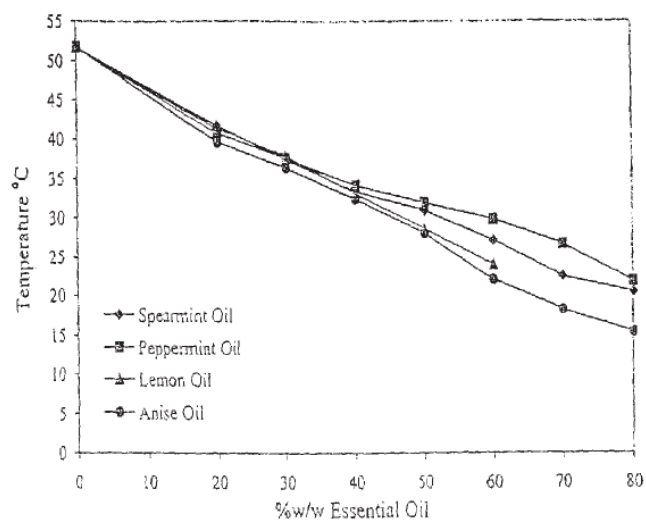


FIG. 4

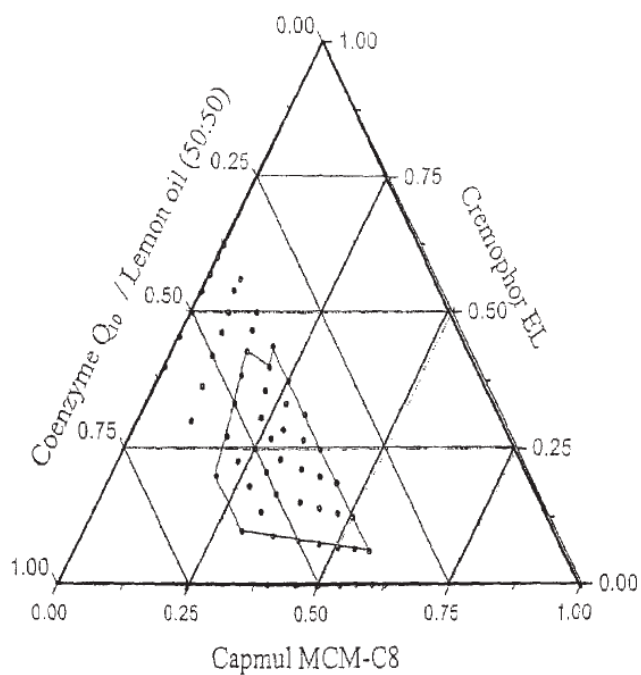


FIG. 5



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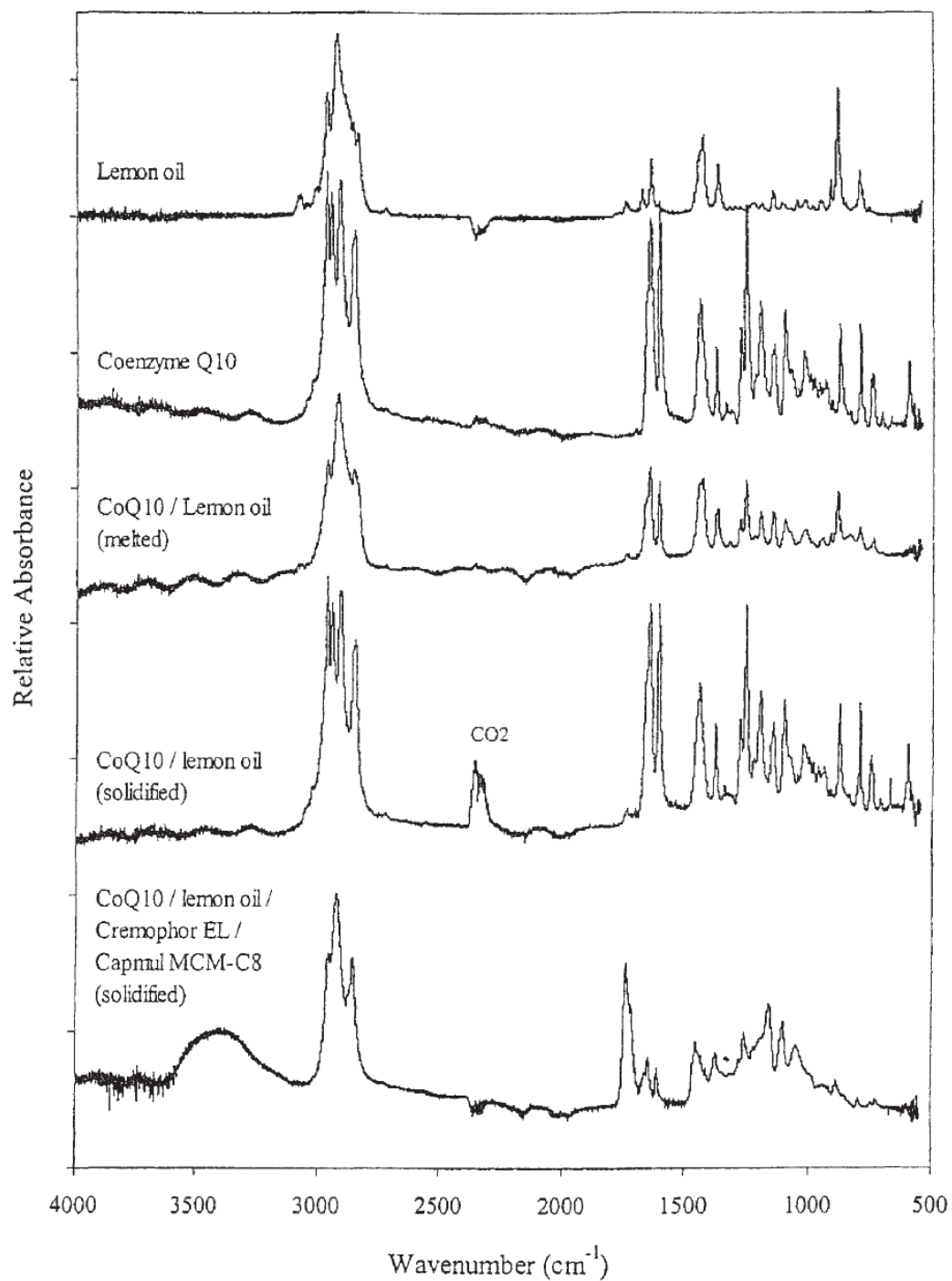


FIG. 7

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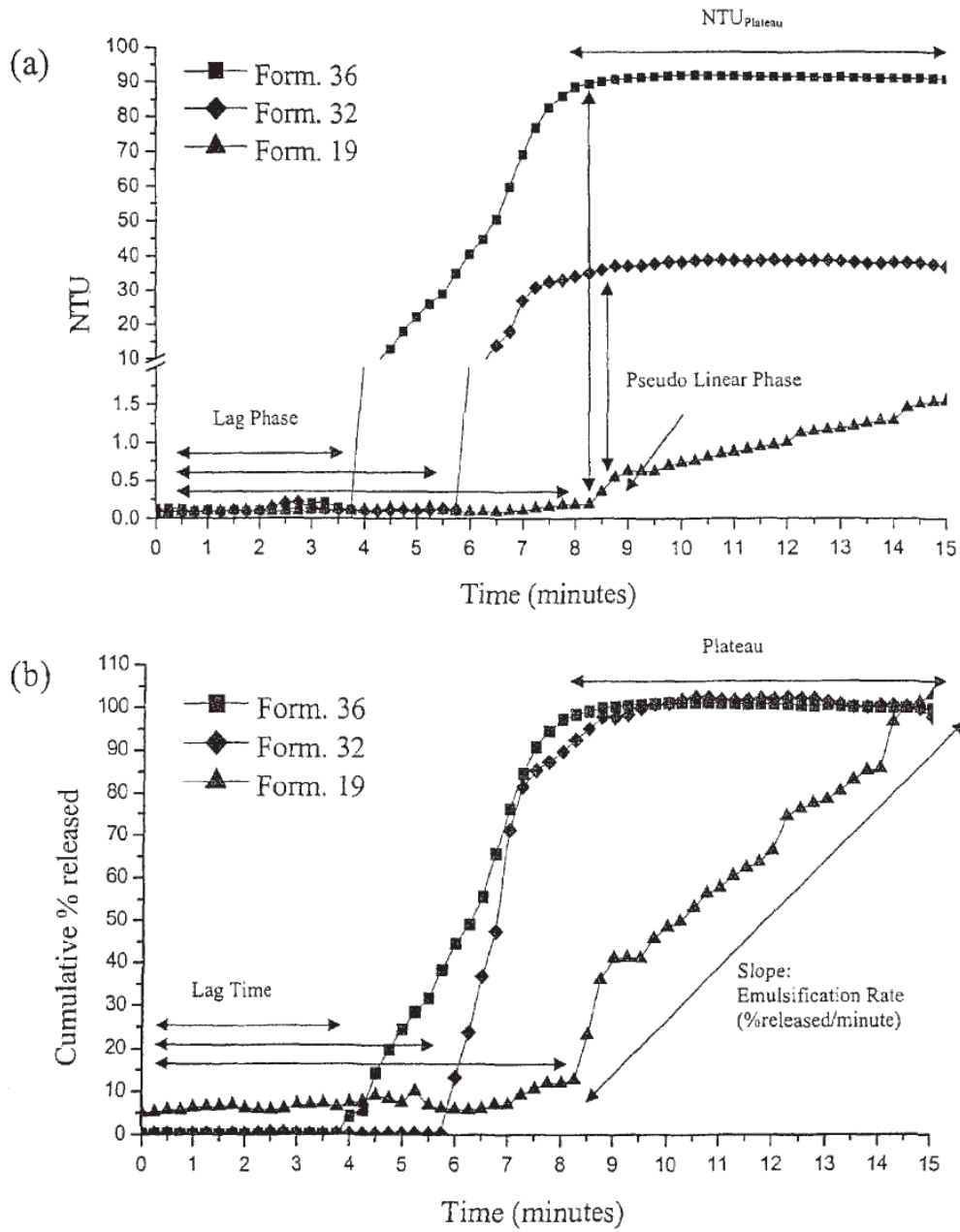


FIG. 8

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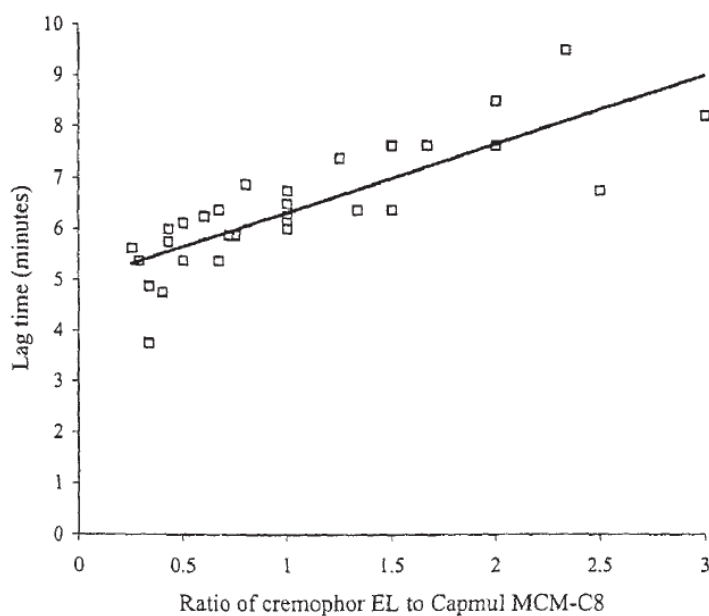


FIG. 9

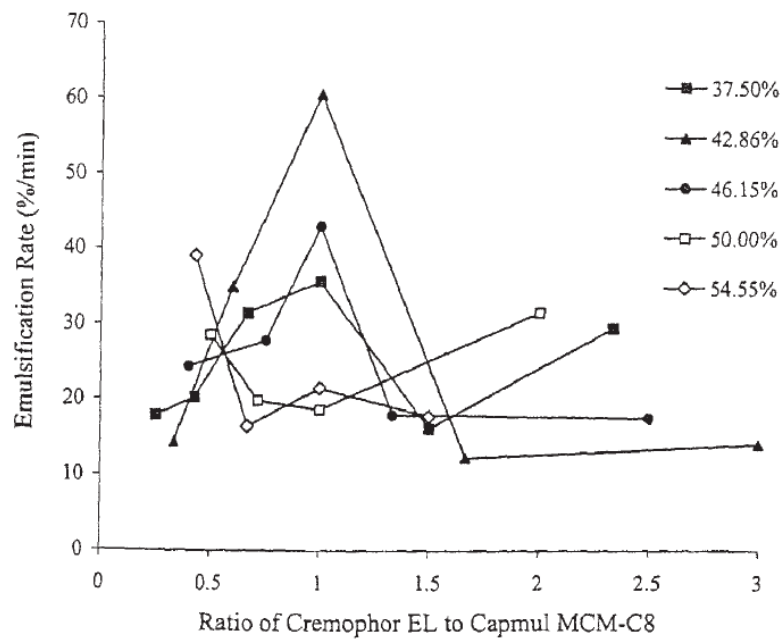


FIG. 10

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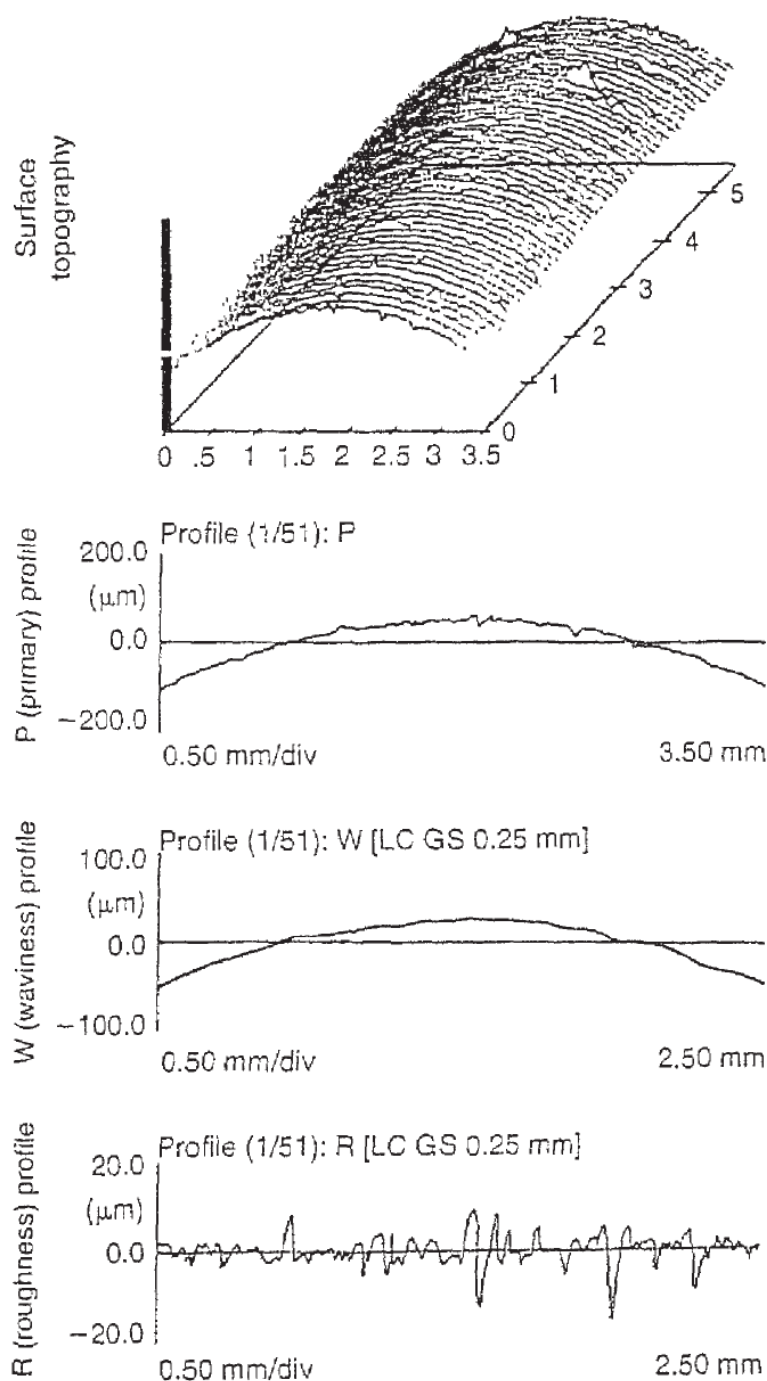


FIG. 12

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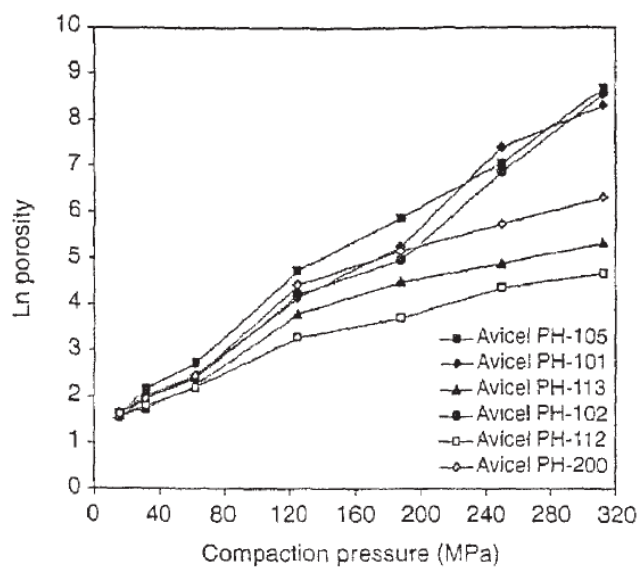


FIG. 13

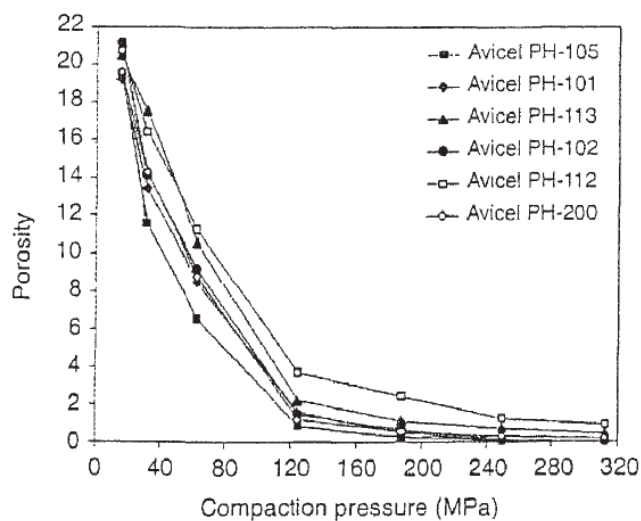


FIG. 14



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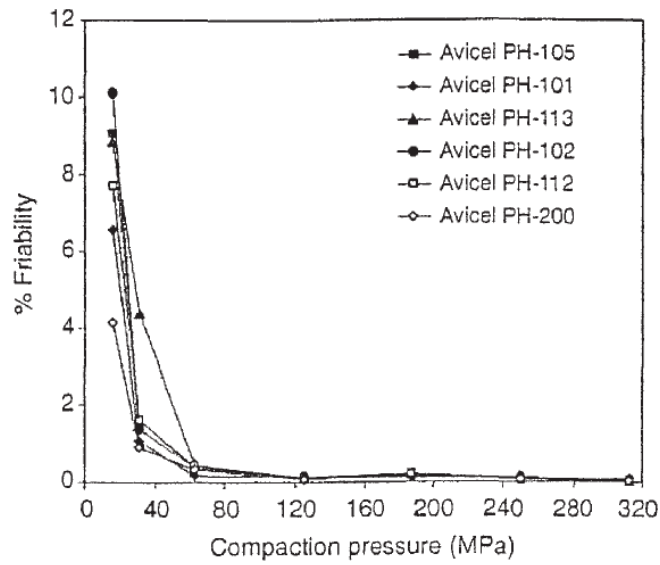


FIG. 17

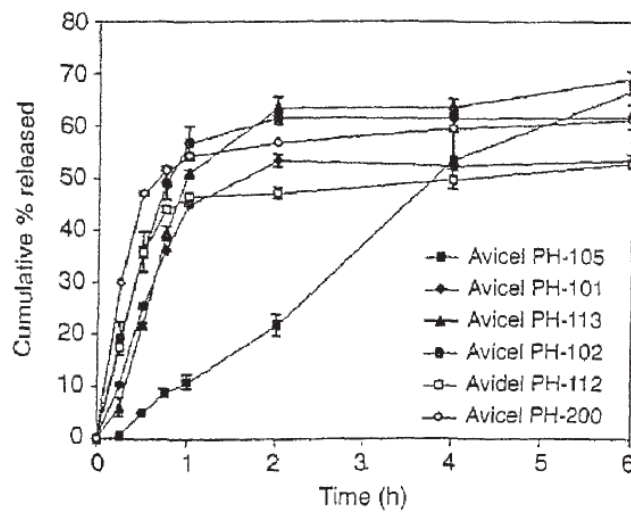


FIG. 18

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**EUTECTIC-BASED SELF-NANOEMULSIFIED
DRUG DELIVERY SYSTEM****CROSS-REFERENCE TO RELATED
APPLICATIONS**

This application claims the benefit, under 35 U.S.C. 119 (e), of U.S. Provisional Application No. 60/331,292 filed Nov. 14, 2001, the contents of which are incorporated herein by reference.

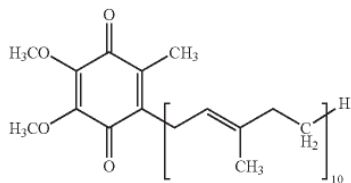
BACKGROUND OF THE INVENTION**1. Field of the Invention**

The present invention relates generally to a eutectic-based self-nanoemulsified drug delivery system (herein referred to as "SNEDDS"). The eutectic-based SNEDDS is preferably used to administer poorly water soluble drugs to a patient.

2. Description of Related Art

Large proportions of new drug candidates have poor water solubility. To overcome these problems, various formulation strategies were reported, including complexation with cyclodextrin, solid dispersions and co-precipitates. In recent years, however, much attention has been focused on lipid based formulations, with particular emphasis on self-emulsifying drug delivery systems (herein referred to as "SEDDS"). SEDDS are isotropic mixtures of oil, surfactant, co-surfactant and drug that form fine oil-in-water emulsion when introduced into aqueous medium under gentle agitation.

Ubiquinone, also known as Coenzyme Q₁₀ (herein referred to as "CoQ₁₀"), is an important component of the mitochondrial respiratory chain. The structure of CoQ₁₀ is as follows:



Because of its poor water solubility, CoQ₁₀ presents a challenge when developing a formulation for oral administration. Many approaches have been used to improve the in vitro dissolution of CoQ₁₀. Some of the approaches include complexation with cyclodextrins, solubilization in a blend of polysorbate 80 and medium chain triglycerides, preparation of redispersible dry emulsion, solid dispersion, and recently, development of a self-emulsified drug delivery system (SEDDS).

In the traditional methods of preparing self-emulsified delivery systems, active ingredients are dissolved in fixed oils or triglycerides and subsequently blended with suitable solubilizing agents. However, due to limited solubility of some drugs, such as CoQ₁₀, in these oils, such methods often result in low drug loading and suffer from irreversible precipitation of the active ingredient and/or the excipient with time.

Emulsion systems based on a eutectic mixture of lidocaine-prilocaine and lidocaine-menthol were used in preparation of topical formulations. However, little is known about the use of eutectic mixtures for the preparation of self-emulsified formulation.

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Formulations containing SEDDS also require filling into soft or hard gelatin capsules. Therefore, the incorporation of self-emulsifying vehicles into a powder to produce solid dosage forms would be of great interest. Recently, pellets containing a self-emulsifying mixture were prepared by extrusion-spheronization. Solid-state microemulsion for the delivery of cyclosporin also was prepared by coating the premicroemulsion with an enteric material. Similarly, a solvent-evaporation method was used to prepare tocopheryl nicotinate tablets using calcium silicates as the adsorbing agent. Such methods often require elaborate processing and instrumentation.

On the other hand, solid solutions and liquisols were produced by blending liquid medications with selected powder excipients to produce free-flowing, readily compressible powders. Such excipients include cellulose or lactose as the carriers and fine silicates as the coating material. Using a similar approach, a solid dosage form based on microemulsion adsorbed onto colloidal silicon dioxide and microcrystalline cellulose was introduced. In most cases as well as in the case of liquisols, however, adsorbed oil- or lipid-based formulations form a thin film of oil on the surface of the powder. This film causes particles to adhere and produces a mass that exhibits poor flow and tableting characteristics. To improve flow and compaction properties, oil loading is reduced, or fine particulates such as silicates are added in quantities often exceeding the limits stated by the Code of Federal Regulations.

BRIEF SUMMARY OF THE INVENTION

To overcome the foregoing problems, a eutectic-based semisolid self-nanoemulsified drug delivery system (SNEDDS) was formed as an alternative to the conventional self-emulsifying vehicles. The SNEDDS contains polyoxyl 35 castor oil (herein referred to as "Cremophor") as a surfactant, a medium chain mono- and diglyceride (herein referred to as "Capmul") as a co-surfactant, essential oils, and a pharmacologically effective drug. The preferred amount of Cremophor is 23-31 wt %. The preferred amount of Capmul is 23-31 wt %. The preferred amount of essential oils is 19-26 wt %. The preferred amount of the pharmacologically effective drug is 19-26 wt %. The essential oils are preferably volatile oils selected from the group comprising menthol, spearmint oil, peppermint oil, lemon oil, anise oil and mixtures thereof. Preferably, the pharmacologically effective drug is a drug having poor water solubility. The preferred pharmacologically effective drug is ubiquinone (herein referred to as "CoQ₁₀"). The SNEDDS is in the form of a semi-solid mass that is then introduced into soft or hard gelatin capsules.

A SNEDDS contains an isotropic mixture of oil, surfactant, co-surfactant and drug, which forms a fine oil-in-water emulsion when introduced into an aqueous medium under gentle agitation. In a eutectic-based SNEDDS, the melting point depression method allows the oil phase containing the drug itself to melt at body temperature from its semisolid consistency and disperse to form emulsion droplets in nanometer size range. The SNEDDS improves the dissolution of poorly soluble compounds, such as the preferred CoQ₁₀.

The SNEDDS may be further incorporated into a powder to produce a solid dosage form. The solid dosage form contains the SNEDDS and the following powdered ingredients: a copolymer of vinylpyrrolidone and vinyl acetate (herein referred to as "Kollidon VA 64"), maltodextrin and microcrystalline cellulose (herein referred to as "MCC"). The pow-

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der ingredients are added to the SNEDDS to provide a solid dosage form having preferably 3-35 wt. % Kollidon VA 64, 35-82 wt. % maltodextrin, 11-47 wt. % MCC and an effective amount of a SNEDDS for administering said pharmacologically effective drug to a patient.

In a preferred embodiment, when eutectic-based SNEDDS of CoQ₁₀ are mixed with small quantities of the Kollidon VA 64 a wax-like copolyvidone paste is formed. Kollidon VA 64 possesses a unique dry-binding capacity. Copolyvidone paste ground with a suitable excipient produces granules with good flow properties that are readily available for direct compression. Maltodextrin was found to be a good grinding agent due to its solubility, particle size, and acceptable adsorbing properties. When compressed, however, the given mixture of the copolyvidone paste and maltodextrin produced soft compacts. Therefore, directly compressible microcrystalline cellulose was added. MCC often is regarded as one of the best excipients for direct compression. Extragranular MCC was shown to increase dissolution rates and compressibility of tablets made by high-shear granulation.

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

The features and advantages of the present invention will become apparent from the following detailed description of a preferred embodiment thereof, taken in conjunction with the accompanying drawings, in which:

FIG. 1 shows DSC thermograms of CoQ₁₀, L-menthol, and their binary mixtures (ratios by weight);

FIG. 2 is a temperature/composition phase diagram of CoQ₁₀-menthol binary system determined by DSC;

FIG. 3 shows DSC thermograms of CoQ₁₀, peppermint oil, and their binary mixtures (ratios by weight);

FIG. 4 is a temperature/composition phase diagram of CoQ₁₀-essential oil binary systems determined by DSC;

FIG. 5 is a pseudo-ternary phase diagram indicating the efficient self-emulsification region;

FIG. 6 is a graph showing the effect of surfactant (cremophor EL) to co-surfactant (capmul MCM-C8) ratios on mean droplet size diameter and on NTU_{observed} and NTU_{plateau} turbidity values;

FIG. 7 shows the FT-IR spectra of CoQ₁₀ and lemon oil, and the effect of re-crystallization on the IR spectra of different CoQ₁₀ mixtures;

FIG. 8 shows turbidity-time profiles: a) turbidity-time profile of three CoQ₁₀ SNEDDS preparation and b) normalized turbidity-time profiles showing the cumulative percent of CoQ₁₀ released with time for the three CoQ₁₀ SNEDDS preparations;

FIG. 9 is a graph showing the effect of surfactant (cremophor EL) to co-surfactant (capmul MCM-C8) ratios on lag time to self-emulsification;

FIG. 10 is a graph showing the effect of surfactant (cremophor EL) to co-surfactant (capmul MCM-C8) ratios on the emulsification rate;

FIG. 11 is a representative load-displacement curve obtained from a three-point flexure test of self-nanoemulsified tablet dosage form;

FIG. 12 is a representative surface topography, P, W, and R profiles of self-nanoemulsified tablets, obtained by a Mahr perthometer concept surface-measuring instrument;

FIG. 13 is an out-of-die Heckel plot of six formulations showing the influence of the added Avicel MCC;

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FIG. 14 is a plot of tablet porosity against compaction pressure showing the compressibility of six self-nanoemulsified powdered formulations with various grades of Avicel MCC;

FIG. 15 is a plot of the natural logarithm of tensile strength against porosity showing the compactibility of six self-nanoemulsified powdered formulations with various grades of Avicel MCC;

FIG. 16 is a plot of tensile strength against compaction pressure showing the tabletability of six self-nanoemulsified powdered formulation with various grades of Avicel MCC;

FIG. 17 is a plot of the percent friability against compaction pressure of six self-nanoemulsified powdered formulations with various grades of Avicel MCC; and

FIG. 18 is a dissolution plot showing the cumulative percent of CoQ₁₀ release with time from six self-nanoemulsified tablet formulations with various grades of Avicel MCC.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed to a eutectic-based self-nanoemulsified drug delivery system (herein referred to as "SNEDDS") containing an isotropic mixture of oil, surfactant, co-surfactant and a pharmacologically effective drug. The oil present in the SNEDDS is an essential oil that is a volatile oil, preferably selected from the group comprising menthol, spearmint oil, peppermint oil, lemon oil, anise oil and mixtures thereof. The essential oils in the SNEDDS are present in a preferred amount of 19-26 wt. %. The pharmacologically effective drug present in the SNEDDS is preferably a poorly water soluble compound, preferably selected from the group comprising drugs or dietary supplements, or nutraceuticals with a log p value over 3. Most preferably, the pharmacologically effective drug is ubiquinone (herein referred to as "CoQ₁₀"). Other preferred pharmacologically effective drugs include, but are not limited to, cyclosporines and Vitamin E. The preferred amount of the pharmacologically effective drug in the SNEDDS is 19-26 wt. %. The surfactant in the SNEDDS is preferably polyoxyl 35 castor oil (herein referred to as "Cremophor") in a preferred amount of 23-31 wt. %. The co-surfactant in the SNEDDS is preferably a medium chain mono- and diglyceride (hereafter, "Capmul") in a preferred amount of 23-31 wt. %. The preferred ratio of Cremophor to Capmul is 0.5-1.5. A preferred SNEDDS containing 23 wt. % lemon oil, 23 wt. % CoQ₁₀, 27 wt. % Cremophor, and 27 wt. % Capmul releases 93.4% CoQ₁₀. The SNEDDS produces a semi-solid mass which is filled into soft or hard gelatin capsules. In a preferred embodiment, the SNEDDS are filled into hydroxypropyl methylcellulose (HPMC) capsules.

The SNEDDS may be further incorporated into a powder to produce a solid dosage form by combining the SNEDDS with the following powder ingredients: a copolymer of vinylpyrrolidone and vinyl acetate (herein referred to as "Kollidon VA 64"), maltodextrin and microcrystalline cellulose (herein referred to as "MCC"). The preferred MCC is Avicel MCC, which is available in many grades that differ from each other by their particle size, particle shape, and moisture content, obtained from FMC Corp. (Newark, Del.). Table 1 shows the physicochemical properties of the preferred Avicel MCC. Avicel PH 105 produces a sustained release tablet dosage form.

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TABLE 1

Avicel MCC Grade	Average Particle Size (μm)	Moisture Content (%)
Avicel PH-105	20	≤ 5
Avicel PH-101	50	≤ 5
Avicel PH-113	50	≤ 2
Avicel PH-102	90	≤ 5
Avicel PH-112	90	≤ 1.5
Avicel PH-200	180	≤ 5

Various MCC grades with different particle size and moisture contents vary in their adsorbing capacity, as shown below in the preferred embodiment illustrated in Example II. Although an MCC with a smaller particle size such as Avicel PH-105 provides a greater surface area for oil adsorption, it shows a reduction in compatibility and tensile strength. On the other hand, Avicel PH-112, which has larger particles and reduced adsorbing capacity, demonstrated improved hardness and compaction. The initial size of the particles constituting a powder is an important factor in determining its compaction behavior. For most powdered materials, compaction of the small particles results in stronger tablets because of the large surface area available for bonding. The powder ingredients are added to the SNEDDS to provide a solid dosage form having preferably 3-35 wt. % Kollidon VA 64, 35-82 wt. % maltodextrin, 11-47 wt. % MCC, and an effective amount of a SNEDDS for administering said pharmacologically effective drug to a patient. In a preferred embodiment, the optimum amount of SNEDDS added to a solid dosage form is determined by maximizing the amount of the pharmacologically effective drug emulsified into a dissolution medium within 45 minutes. In a preferred embodiment wherein CoQ₁₀ is the pharmacologically effective drug, 46.1-91.1 wt. % CoQ₁₀ was released from the solid dosage form within 45 minutes. A preferred solid dosage form containing 7.8 wt. % Kollidon VA 64, 65.4 wt. % maltodextrin, 11.7 wt. % MCC, and 15.1 wt. % SNEDDS release 85.4% of CoQ₁₀. The SNEDDS is this preferred solid dosage form contained an oily mix of CoQ₁₀ and lemon oil in a ratio of 1:1. Cremophor EL and Capmul MCM-C8 were added to the oily mix at a final concentration of 26.9% w/w each.

EXAMPLE I

The present example illustrated the use of eutectic mixtures with essential oils for the preparation of SNEDDS. Prepared SNEDDS improve the dissolution of poorly water soluble drugs, such as CoQ₁₀. Recrystallization adds to the stability of the drug while providing attractive semisolid preparation that could be filled into hard capsules. Turbidimetry directly correlates emulsification rate, lag times and droplet size with formulation ingredients. This was used to distinguish between different self-emulsified preparations, which might be more important than simply identifying systems that are spontaneously emulsifying.

Differential Scanning Calorimetry (DSC) of CoQ₁₀-Menthol and CoQ₁₀-Essential Oil Binary System.

CoQ₁₀ and L-menthol were mixed at various ratios between 90:10 and 10:90 (w/w). Approximately 5 mg of the mixture was sealed in an aluminum pan and analyzed using a differential scanning calorimeter (DSC 7, Perkin-Elmer, Norwalk, Conn.). Thermal analysis was carried out between 25 and 60° C. under nitrogen gas flow against an empty reference pan at a heating rate of 10° C. min⁻¹. Similarly, different ratios of CoQ₁₀ and the essential oil between 80:20 and 20:80

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(w/w) were mixed and melted at 37° C. Resulting oils were stored at 4° C. for 24 hours to allow complete re-crystallization of CoQ₁₀. To avoid oil evaporation, approximately 10 mg of the mixture was weight onto a DSC sample pan and kept in an airtight container during storage prior to DSC analysis. For CoQ₁₀-essential oil mixtures at ratios between 80:20 and 60:40 (w/w), thermal analysis was carried out between 25 and 55° C. Heating rate used was 10° C. min⁻¹. Lower temperatures were maintained using refrigerated cooling accessory (Intracooler 2, Perkin-Elmer).

CoQ₁₀ was found to form a eutectic mixture with L-menthol. DSC thermograms of the binary system of CoQ₁₀ with menthol at different ratios are given in FIG. 1. The major endotherms at 51.7 and 44.1° C. represent the melting point of CoQ₁₀ and L-menthol, respectively. Based on the thermal analysis data a binary phase diagram was constructed and is given in FIG. 2. As seen from FIG. 2, the eutectic melting point lies between 30 and 60% w/w CoQ₁₀. Within the binary system, depression in melting temperature of CoQ₁₀, however, was limited to temperatures exceeding 37° C. Thus, an oily melt can not be obtained at or below body temperature. A gradual shift and reformation of the original CoQ₁₀ endothermic peak was observed when the samples within the binary system were left uncovered and analyzed after 1 week. The volatile ingredients of menthol are responsible for the physical changes in CoQ₁₀, i.e. depression in its melting temperature. To validate this observation, the effect of peppermint oil as a representative volatile ingredient of menthol crystals and three additional volatile oils namely, spearmint oil, lemon oil and anise oil were investigated for their effect on the melting thermograms of CoQ₁₀. Thermal analysis and the DSC data of the binary system of CoQ₁₀ with peppermint oil are given in FIG. 3. A binary phase diagram of CoQ₁₀ with the essential oils was constructed and is given in FIG. 4. Thermograms of the mixtures clearly indicated that these compounds formed binary eutectic systems. An increase in percent essential oil causes a gradual decrease in the melting temperature of CoQ₁₀. At sufficient concentration of the volatile oil it becomes feasible to convert CoQ₁₀ into an oily phase at or below body temperatures.

Determination of CoQ₁₀ Melting Time

CoQ₁₀ was accurately weighed and mixed with 50 and 60% w/w of peppermint oil, spearmint oil, anise oil or lemon oil in a screw-capped glass vials. Mixtures were allowed to melt at 37° C. in water bath (Ikamag® Ret-G, Terochem Scientific, Toronto, Canada). Cremophor EL was added to the melt at a concentration of 20, 40 and 60% w/w of the final weight using a positive displacement pipette (Microman®, Gilson Inc., Middleton, Wis.) and stirred with a magnetic bar. Vials were then capped and stored at ambient temperatures in tight containers protected from light. After 24 hours sample vials containing the solidified preparation were immersed in water bath maintained at 37° C. Samples were monitored for a change in their physical appearance and the time was recorded until a complete melt was obtained.

Due to the limited solubility of CoQ₁₀ in fixed oils and triglycerides, the melting point depression method using essential oils provides an attractive alternative for the preparation of an emulsified formulation. A number of essential oils are used for their flavors and odors and are recognized by the Code of Federal Regulations as GRAS (generally recognized as safe) compositions that do not require regulatory agency approval before they are included in ingested material. A preparation could be made at which body temperature is used to melt a system comprising essential oil, CoQ₁₀ and an emulsifier when the essential oil is added in an amount

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sufficient to lower the melting temperature of CoQ₁₀ to or below 37° C. Essential oils, however, should be effective as eutectic agents in the presence of other liquid excipients. Table 2 demonstrates the feasibility of the described approach by showing the melting time, in minutes, for the given mixture of CoQ₁₀, essential oil and cremophor EL at 37° C. Four essential oils, spearmint oil, peppermint oil, lemon oil, and anise oil, were evaluated for their eutectic efficacy in the presence of other formulation excipients. The essential oil percentage rates in Table 2 are the percent w/w of essential oil in the binary mixture of the essential oil with CoQ₁₀. The Cremophor EL (CrEL) percentage rates in Table 2 are the percent w/w of Cremophor EL in the final mixture of CoQ₁₀, essential oil and cremophor EL. The N/A indication in Table 1 indicates the formulations where no melting time was observed within 24 hours.

TABLE 2

CrEL (%)	20%	40%	60%
<u>Spearmint Oil</u>			
60%	0.69 ± 0.13	1.56 ± 0.59	N/A
50%	4.38 ± 2.13	N/A	N/A
<u>Peppermint Oil</u>			
60%	1.11 ± 0.42	N/A	N/A
50%	8.17 ± 2.08	N/A	N/A
<u>Anise Oil</u>			
60%	0.83 ± 0.73	0.97 ± 0.27	N/A
50%	1.28 ± 0.63	2.33 ± 0.88	N/A
<u>Lemon Oil</u>			
60%	1 ± 0.17	1.29 ± 0.44	1.76 ± 0.23
50%	2 ± 0.29	3.56 ± 1.69	5.33 ± 1.48

Due to limited solubility of CoQ₁₀ in surfactant, the use of cremophor EL as a model emulsifier not only induces crystallization of CoQ₁₀ in the cooled supersaturated mixture but also may delay or retard re-melting the system at higher temperatures. The time necessary to melt different combinations of CoQ₁₀, essential oil and cremophor EL at 37° C. was recorded. When 60% w/w of cremophor EL was added, preparations made with 50 and 60% w/w lemon oil to CoQ₁₀ melted within 5.3 and 1.8 min, respectively. Precipitation of CoQ₁₀ at higher cremophor EL concentration for the formulas made with anise oil, peppermint oil and spearmint oils was however irreversible rendering them less effective for the preparation of emulsified systems. The use of lemon oil appears reasonable and attractive. At 50% w/w of lemon oil to CoQ₁₀, formulas would melt within 5 min from initial exposure to body temperatures. In this case, recrystallization of CoQ₁₀ becomes advantageous in the production of a stable semisolid product compared with the existing liquid formulas with the potential of irreversible precipitation and separation of the active ingredient due to supersaturation or fluctuation in storage temperatures. Furthermore, lemon oil has been used internally as herbal medicine for acidic disorders such as arthritis and rheumatism with great benefit in liver congestion.

Visual Observations

To assess the self-emulsification properties, formulation (50 mg) pre-melted at 37° C. was introduced into 100 ml of water in a glass Erlenmeyer flask at 25° C. and the contents were gently stirred manually. The tendency to spontaneously form a transparent emulsion was judged as 'good', and it was judged 'bad' when there was poor or no emulsion formation.

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Phase diagrams were constructed identifying the good self-emulsifying region. All studies were repeated in triplicates with similar observation being made between repeats.

For the development of a self-emulsified formulation, a right blend of low and high HLB surfactants is necessary for the formation of a stable microemulsion. Therefore, a high HLB surfactant, cremphor EL, and a low HLB co-surfactant, capmul MCM-C8, were selected. A ratio of 50:50 of lemon oil to CoQ₁₀ was selected as the oil phase. The pseudo ternary phase diagram of the system comprising the surfactant, co-surfactant and the oily phase was constructed and is given in FIG. 5. The area enclosed within the solid line represents the region of self-emulsification. Within this area a ternary mixture forms a fine oil in water emulsion with only gentle agitation. This is possible as surfactant strongly localized to the surface of the emulsion droplet reduces interfacial free energy and provide a mechanical barrier to coalescence resulting in a thermodynamically spontaneous dispersion. Furthermore, co-surfactants increase interfacial fluidity by penetrating into the surfactant film creating void space among surfactant molecules. Constraints on the formulas were placed so that the oil phase was not less than 37.5% to ensure melting of the crystallized product based on the early predictions give in Table 2, and did not exceed 63% to ensure efficient CoQ₁₀ emulsification.

Emulsion Droplet Size Analysis and Turbidity Measurements

Formulation (50 mg) melted at 37° C. was diluted with water, pre-equilibrated at 37° C., to 100 ml in an Erlenmeyer flask and gently mixed with hand. The resultant emulsions were evaluated for its droplet size and turbidity as follow.

The droplet size distribution of the resultant emulsions was determined by laser diffraction analysis using Coulter particle size analyzer (Model LS230, Miami, Fla.), which has a particle size measurement range of 0.04–2000 μm . The sizing of the emulsions was determined in a small volume module. Samples were directly placed onto the module and the data was collected for 60 seconds. Particle size was calculated from the volume size distribution. All studies were repeated, with good agreement being found between measurements.

Turbidity of the resultant emulsions given in nephelometric turbidity units (NTU) was measured using HACH turbidimeter (Model 2100 AN, Loveland, Colo.). Turbidity measurements were performed on 30 ml of the emulsion stored in a clear screw-capped sample vials. The HACH 2100AN turbidimeter used was carefully calibrated with formalin standards. Accuracy at the lower range of turbidity is essential especially for small and diluted emulsions with high surfactant concentrations. The largest source of error at low turbidities is the stray light, that is, the light that reaches the detector due to sources other than sample turbidity. Accuracy of the HACH 2100AN turbidimeter, as specified by the manufacturer and based on instrument calibration, is approximately ± 0.01 NTU with stray light less than or equal to 0.01 NTU.

The effect of surfactant to co-surfactant ratio on droplet size is given in FIG. 6. At ratios greater than 0.5, globule size was relatively constant at about 100 nm and independent on any component of the ternary system. It was only at ratios smaller than 0.5 when globule size increased and became greatly dependent on cremophor EL and capmul MCM-C8 concentrations yet independent on the added oil phase. It was reported that the addition of surfactant to the microemulsion systems causes the interfacial film to stabilize and condense, while the addition of co-surfactant causes the film to expand. Comparison of droplet size data with the visual observations shows that good emulsification properties are reflected by the low globule size with the exception of the formula made with

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high capmul MCM-C8 to cremophor EL ratios. This reflects the fact that the visual test is a measure of the spontaneity of emulsification rather than a measure of the quality of the formed emulsion.

Turbidity, given in NTU, was measured for the same samples utilized for particle size analysis. The effect of surfactant to co-surfactant ratio of the emulsified formulas on $NTU_{observed}$ and $NTU_{plateau}$ turbidity readings is given in FIG. 6. As seen in the plot, turbidity follows the same trend as droplet size. It has been reported that a linear correlation exists between the intensity of the scattered light and the squared volume of the dispersed droplets. Hence, NTU could be directly used to predict relative droplet size of the emulsion. To give a sense about the clarity of the formulas, turbidity of drinking water ranges from 0 to 1 NTU.

Fourier Transform-Infrared Spectroscopy (FT-IR)

FT-IR spectroscopy was performed using FT-IR model Nicolet Impact 410 (Thermo Nicolet, Madison, Wis.) attached to an attenuated total reflectance (ATR) accessory (DuraSampl/R, SensIR Technologies, Danbury, Conn.). ATR was fitted with a single bounce diamond at 45° internally reflected incident light providing a sampling area of 1 mm in diameter with a sampling depth of several microns. Samples analyzed were CoQ₁₀ powder, a 50:50 CoQ₁₀-lemon oil melt, a solidified 50:50 CoQ₁₀-lemon oil mix and a solidified mixture of lemon oil, CoQ₁₀, cremophor EL and capful MCM-C8 at a ratio of 0.5:0.5:1:1. Samples were prepared as described above. A small amount of the sample was directly placed on the diamond disk and scanned for absorbance over the range from 4000 to 500 wavenumbers (cm⁻¹) at a resolution of 1 cm⁻¹.

The ease of handling aqueous solutions and semisolid preparations is one of the major advantages of ATR used in conjugation with FT-IR spectrometry. CoQ₁₀ compatibility with the excipients of self-nanoemulsified preparation can be tested with FT-IR. Absorbance spectrums of CoQ₁₀ and lemon oil are given in FIG. 7. CoQ₁₀ spectrum showed several sharp characteristic peaks. The spectrum of the 50:50 melt of CoQ₁₀ and lemon oil, given in FIG. 7, had features of each of the components with the expected peak broadening due to its amorphous character whereas a sample of the solidified mixture had sharp lines and resembled the CoQ₁₀ spectrum in every detail. Lemon oil did not change the infrared spectrum of CoQ₁₀ indicating no chemical interaction in the binary system and that the molecular structure of CoQ₁₀ remained completely intact. Similarly, when cremophor EL and capmul MCM-C8 were added to the CoQ₁₀-lemon oil mix and the solidified mixture was analyzed, the resulting spectrum given in FIG. 7 had the characteristic CoQ₁₀ bands at 1608 and 1643 cm⁻¹ corresponding to the benzoquinone ring and the mono substituted isoprenoid units, respectively. The results obtained indicate that CoQ₁₀ reforms to its original crystalline state when the formulation is allowed to solidify.

Dissolution and Emulsification Studies

Dissolution profiles of the capsules filled with the self-nanoemulsified formulations were mined using USP XXIII rotating paddle apparatus (VanKel, mod. VK 7000, Cary, N.C.) at 37° C. and a rotating speed of 50 rpm in a 900 ml of water. Capsules were held to the bottom of the vessel using copper sinkers. Samples (3 ml) withdrawn after 15 min were filtered using a 10 µm VanKel filter and assayed for CoQ₁₀ by the HPLC method reported in the HPLC analysis section. The dissolution experiments were carried out in triplicates.

Turbidity profiles of the capsules filled with the self-emulsified formulations were determined using HACH turbidimeter (Model 2100AN). Low-pressure flow cell was used to

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allow directly reading samples turbidity associated with capsules subjected to the same dissolution conditions as described above. Two 1/8 in. tygon tubing were connected to the pump attached to the dissolution autosampler (VanKel, mod. VK8000). First tubing was installed between the pump and the inlet of the flow cell while the other connected the pump to the dissolution vessel. Inlet of the tube connecting pump to the dissolution vessel was covered with a 40 µm nylon screen and immersed into the medium so that the sample can be continuously withdrawn from a zone midway between the surface of the medium and the top of the rotating blade. Another tubing was installed to the outlet of the flow cell leading back to the dissolution vessel. Before starting, deionized water was pumped through the flow cell until a reading below 0.150 NTU was maintained. Throughout the study, dissolution medium was continuously pumped into the flow cell and back to the dissolution vessel. The turbidimeter was set so that a reading was recorded on the attached printer every 15 seconds. Turbidimetry experiments were carried out in triplicates.

To assess spontaneity and efficacy of emulsification, turbidity of the dispersion and the relative intensity of the scattered light was correlated with time during the emulsification process. Current design confines to the standard compendia requirements for conducting dissolution experiments. Utilizing the flow through attachment, turbidity was directly measured using standard dissolution apparatus at 37° C. and controlled paddle rotating speed. Prepared formulations were filled into hydroxypropyl methylcellulose (HPMC) capsules. HPMC capsules are shown to dissolve at longer times compared with standard gelatin capsules. Average dissolution time for an HPMC capsule size 4, 3 and 0 in water at 37° C. was 300, 250 and 120 s, respectively. Extra time provided by HPMC capsules allows the formula to completely melt at body temperature before its exposure to body fluids. Representative dissolution curves monitored by turbidimetry for three formulations are shown in FIG. 8(a). Formulation 19 has 21.4% w/w CoQ₁₀, 21.4% w/w lemon oil, 14.3% w/w Capmul, and 42.9% w/w Cremophor. Formulation 32 has 27.3% w/w CoQ₁₀, 27.3% w/w lemon oil, 31.8% w/w Capmul, and 13.6% w/w Cremophor. Formulations 36 has 30.0% w/w CoQ₁₀, 30.0% w/w lemon oil, 30.0% w/w capmul, and 10.0% w/w cremophor. Due to large number of readings obtained, plots of turbidity against emulsification time have the characteristic lag phase, pseudo linear phase and a gradual tailing toward a plateau as the emulsion systems approached equilibrium. Actual cumulative amount of CoQ₁₀ released after 15 min for the preparations was measured by HPLC. CoQ₁₀ was completely released and dispersed from all formulations into the medium within 15 minutes.

CoQ₁₀ was analyzed at ambient temperature utilizing a C18, 3.9×150 mm reverse phase chromatography column (Nova-Pak; Waters, Milford, Mass.). The mobile phase consisted of methanol:n-hexane (9:1) and was pumped at a flow rate of 1.5 ml min⁻¹. The Waters HPLC instrument consisted of a 510 pump, 712 WISP autosampler, and a 490E UV detector set at a wavelength of 275 nm. The chromatographic data was managed using STAR 5.3 software (Varian, Walnut Creek, Calif.).

NTU values obtained for the solidified samples placed in the dissolution medium at 37° C. after reaching an equilibrium could be termed $NTU_{plateau}$. In order to demonstrate the efficacy of emulsion formation before and after solidification $NTU_{observed}$, which were previously determined for the melted samples while measuring droplet size, could be roughly correlated with $NTU_{plateau}$.

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Lag phase of the turbidity-time profile reflects the time elapsed before the formula is released from the capsule into the dissolution medium. FIG. 9 correlates lag times with surfactant to co-surfactant ratios. Intercept of the regression line with the y-axis was at 4.98 min which is almost identical to the average break time for an empty HPMC capsule size 4. Any deviation from this time should be correlated with the inherent properties of the fill material. Increase in cremophor EL to capmul MCM ratios from 0.5 to 3 delayed the onset of emulsion formation from 6.1 to 8.2 min, respectively. Increase in surfactant concentration delayed the onset of emulsification. At high cremophor EL concentration, progress of emulsification might be compromised by viscous liquid crystalline gel formed at the surfactant-water interface. It was reported that when a self-emulsified system is diluted by the aqueous phase various mesomorphic phases formed between the formula and the water. This was observed when the mesogenic properties of the formulation at different concentrations of each component were evaluated by studying the optical birefringence of the samples. In the absence of water, a droplet of surfactant (cremophor EL) and co-surfactant (capmul MCM-C8) placed in contact on a microscope slide revealed a boundary with no obvious signs of mixing and no optical birefringence. When cremophor EL was mixed with water in the absence of co-surfactant, the mixture showed birefringent texture of a gel. Addition of co-surfactant resulted in typical birefringent textures of non-gelled fluid lyotropic liquid crystalline phase for a system with a fixed surfactant to co-surfactant weight ratio of 1:1.

As shown in FIG. 8(b), a cumulative percent of the formulation emulsified with time could be obtained by plotting cumulative $NTU_{plateau}$ as a function of time, assuming that $NTU_{plateau}$ reflect 100% of the formula released from the capsules regardless of the actual amount of CoQ_{10} dissolved in the medium. As seen from FIG. 8(b), plots of cumulative percent of the formulation released with time are identical to the original profiles correlating turbidity with time where curved characteristics mainly lag time, pseudo linear phase and plateau are preserved. This, slope of the pseudo linear phase for the line correlating cumulative percent emulsified with time could be regarded as the emulsification rate (E_{rate}) or emulsification efficacy. This value is very useful in comparing emulsification tendency of the self-emulsified preparation. FIG. 10 correlates emulsification rate with oil loading and surfactant to co-surfactant ratios. E_{rate} is given as percent of the formula emulsified per minute. Maximum emulsification rate was obtained at a surfactant to co-surfactant ratio of 1 and oil loading of 42.6%.

EXAMPLE II

Powdered self-emulsified dosage forms provide an attractive alternative to filled-capsule preparations. The proper excipient selection, however, is crucial when formulating dry adsorbed solid formulations. The following example illustrates the various properties associated with a preferred powdered self-emulsified dosage form.

Preparation of a Solid-State Self-Nanoemulsified Dosage Form

The eutectic-based self-nanoemulsified drug delivery system (SNEDDS) of CoQ_{10} was prepared as follows: CoQ_{10} and lemon oil at a ratio of 1:1 were accurately weighed into screw-capped glass vials and melted in a water bath at 37° C. Cremophor EL and Capmul MCM-C8 were added to the oily mix, each at a final concentration of 26.9% w/w. The resultant emulsion was mixed with a stirring bar until a transparent

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solution of SNEDDS was obtained. The SNEDDS then was allowed to cool at ambient temperature for 24 hours until a viscous paste was obtained. Nanoemulsion-adsorbed granular material was obtained from a mixture of SNEDDS paste, Kollidon VA 64, Glucidex IT 12, and Avicel at a ratio of 0.11:0.13:0.56:0.2, respectively. SNEDDS was mixed initially with Kollidon VA 64 using a mortar and pestle until a semisolid waxy paste was obtained. The mixture then was ground with Glucidex IT 12 in the mortar for 1 min to obtain the dry microemulsion-based granules. Finally, Avicel was added to the granules and blended in a V-blender (Patterson-Kelley Co., E. Stroudsburg, Pa.) for 5 minutes. Six formulations were made, each with a different grade of Avicel MCC.

Carr's Flowability Index

The flow properties of the solid-state powdered emulsion were determined by Carr's method. Compressibility, angle of repose, angle of spatula, and uniformity coefficient were measured.

The granular powder (10 g) was poured lightly into a 25-mL graduated cylinder. The powder was tapped until no further change in volume was observed. Powder bulk density, ρ_b (g/cm³), was calculated as the weight of the powder divided by its volume before tapping. Powder tapped density, ρ_p (g/cm³), was calculated as the weight of the powder divided by its volume after tapping. The percentage of compressibility was computed from the following equation:

$$\% \text{ compressibility} = 100 \left(\frac{\rho_p - \rho_b}{\rho_p} \right)$$

The angle of repose was measured with a protractor for the heap of granules formed by passing 10 g of the sample through a funnel at a height of 8 cm from the horizontal surface. A steel spatula with a 5×7/8 in. blade was inserted to the bottom of the heap and withdrawn vertically. The angle of the heap formed on the spatula was measured as the angle of spatula.

The uniformity coefficient was obtained by sieve analysis of 10 g of the powdered material using a Retsch sieve shaker type AS200 (F. Kurt Retsch GmbH, Germany) fitted with eight US-standard sieves (Dual Mfg. Co., Chicago, Ill.) ranging in size from 0.075 to 1.7 mm. Uniformity coefficient is the numerical value arrived at by dividing the width of the sieve opening that will pass 60% of the sample by the width of the sieve opening that will pass 10% of the sample. The flowability index was calculated with the point scores, ranging from 0 to 100, in a scale described by Carr to evaluate the flow and the arching properties of powders.

Compaction of the Solid-State Self-Nanoemulsified Dosage Form

Microemulsion-adsorbed compacts were prepared using concave elongated punches (Natoli Engineering Co., St. Charles, Mo.). Tablets were made by compressing 1245 mg of the powder, which corresponds to 30 mg in weight of CoQ_{10} , between the faces of the punch. Punches were mounted between the platens of a Carver press model C (Carver Inc., Wabash, Ind.) attached to a semiautomatic compression assembly model 2826 (Carver). The compaction pressure ranged from 15.6 to 312.3 MPa. The dimensions of the compact were measured to ±0.01 mm using a dial thickness gauge (Lux Sci. Inst. Corp., New York, N.Y.). Punches were 0.750 in. long and 0.375 in. wide and provided tablets with an area of the curved segment equivalent to 0.0083 in.² and a height of the curved surface above the central thickness equivalent to 0.06 in.

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Determination of True Density and Compact Porosity

The true density, ρ_t , of the powdered self-emulsified formulation was determined in triplicate using a helium pycnometer, model Ultra-pycnometer 1000 (Quantachrome, Boynton Beach, Fla.). The density of the resulting compacts, ρ_c , was calculated from the weight and volume of the compact. The porosity, ϵ , of the compacts was calculated by the following equation:

$$\epsilon = 100 \left(1 - \frac{\rho_c}{\rho_t} \right)$$

Determination of Tensile Strength

Tensile strength provides a measure of the inherent strength of the compacted material independent of tablet dimensions. Tensile strength of the elongated, curve-faced tablets was measured in triplicate with a three-point flexure test using the Instron material-testing instrument model 4442 (Instron Corp., Canton, Mass.). The load was applied at a rate of 25 mm/min, and the fracture load was obtained from the load-displacement curve recorded using Instron software series IX. A typical load-displacement curve of the microemulsion-based tablets is shown in FIG. 11. Tablets were examined for the mode of failure, and only those with the fracture plane running through the center point of the surface of the tablet were used to derive tensile-strength values.

The tensile strength was calculated by the following equation:

$$\sigma_f = \frac{3FL}{2d^2} \left(\frac{d+2a}{6A+bd} \right)$$

in which σ_f is the tensile strength; F is the fracture load in a three-point flexure test; b and d are the width and the thickness of the tablet, respectively; a is the height of the curved surface above the central thickness; A is the area of the curved segment; and L is the distance between the lower supports.

Heckel Analysis

The densification of the dry powdered emulsion was analyzed by the out-of-die Heckel equation

$$-L \ln \epsilon = KP + D$$

in which P is the compaction pressure, ϵ is the porosity of the compact, K is the slope of the linear portion of the Heckel plot, and D is a function of the original compact volume. K is equal to the reciprocal of the mean yield pressure P_y , which is three times the yield strength of the material. D is a constant related to the geometry of the system and the degree of packing of the particles in the die.

Measurement of Surface Roughness

The roughness profiles for the upper and lower surfaces of the compacts were measured with a Mahr perthometer con-

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cept 6.3 surface texture-measuring instrument (Mahr Federal Inc., Cincinnati, Ohio). Tablets were mounted on the X/Y table and scanned with a contact PZK drive unit using the stylus method to move the tracing arm (model MFW-250) across the surface. A tracing length of 3.5 mm was used to obtain 51 profiles with a spacing of 112 μ m. P-profile, waviness, and roughness parameters were computed for every profile, and the mean of all 51 profiles was collected. The following parameters were measured:

10 P_s (profile parameter): the mean distance between local peaks of the P-profile

W_s (waviness parameter): the mean distance between local peaks of the W-profile

15 R_a (roughness average): the arithmetic average of the roughness profile ordinates

R_z (mean roughness depth of the R-profile): the arithmetic average of roughness depths (i.e., the vertical distance between the highest peak and the deepest valley of consecutive sampling lengths).

20 P -profile (primary profile): the mean line generated from the traced profile. Using profile filters, P-profiles separate into long-wave (W-profile) and short-wave (R-profile) components. A representative surface topography, P, W, and R profiles, obtained by the profilometer are shown in FIG. 12.

Friability and Disintegration Studies

The friability of the compacts was measured using a VanKel type, dual-chamber drum, friability tester (VanKel, Cary, N.C.) set at a rotation speed of 25 rpm. Five grams of tablets were rotated for 4 min (100 rotations). At the end of the run the tablets were weighed accurately, and the percent friability was computed from the weight of tablets before and after the test. The disintegration time for three replicates was measured using the VanKel single-basket disintegration-testing system at 37° C. according to the USP XXIV specification.

Dissolution Studies

The dissolution profiles of the self-emulsified tablets were determined using a USP XXIV rotating basket apparatus (model VK7000, VanKel) at 37° C. The rotating speed was 50 rpm, and the dissolution medium was 900 mL of water. Samples (3 mL) withdrawn at fixed time intervals were filtered using a 10- μ m VanKel filter and were assayed for CoQ₁₀ by HPLC at 275 nm. Briefly, CoQ₁₀ was analyzed using a C18 3.9x150 mm reverse-phase chromatography column (Nova-Park; Waters, Milford, Mass.). The mobile phase consisted of methanol-n-hexane (9:1) and was pumped at a flow rate of 1.5 mL/min⁻¹. The dissolution experiments were conducted in triplicate.

Evaluation of Flow Properties

One of the limitations of self-emulsified tablet dosage forms is the poor flow of the powdered mass that holds the oily formulation. The flowability index shown in Table 3 for the microemulsion-absorbed powdered material was obtained by measuring the powders' mechanical properties (i.e., compressibility, angle of repose, angle of spatula, and uniformity coefficient as previously discussed).

TABLE 3

Grade	Disintegration Time (min)	Tensile Strength		Yield Strength		Flowability Index
		σ_0 (MPa)	R ²	(MPa)	R ²	
Avicel PH-105	47.82 (0.66)	0.26098	0.987	14.3062	0.994	56.5
Avicel PH-101	30.65 (0.65)	0.35876	0.989	14.368	0.992	63.5

TABLE 3-continued

Avicel MCC	Disintegration	Tensile Strength		Yield Strength		Flowability
Grade	Time (min)	σ_0 (MPa)	R ²	(MPa)	R ²	Index
Avicel PH-113	27.88 (1.5)	0.32991	0.997	25.0627	0.948	59
Avicel PH-102	22.775 (1.275)	0.32834	0.991	14.43	0.991	55
Avicel PH-112	23.475 (1.975)	0.38837	0.992	30.8642	0.97	63
Avicel PH-200	15.94 (1.54)	0.34455	0.992	20.202	0.951	52

According to the method proposed by Carr, the flowability performance of a powder with a flow index between 60 and 69 can be described as acceptable. A higher value would indicate a still-better flow, but considering high oil loading in the formulation, the flow values obtained are reasonably good. For direct compression, these values can be improved readily by adding a low concentration of silicates such as silicon dioxide, commonly used as a glidant and anti-adherent. Good flow is the result of the granular nature of the formulations, which is enhanced primarily by the absorbing properties of Kollidon VA 64. The effect of MCC particle size on the flow properties of the preparations appeared insignificant.

Heckel Analysis of the Powdered Self-Emulsified Formulation

The Heckel equation is used often to distinguish between the mechanisms of consolidation such as plastic deformation and brittle fracture. Three types of Heckel plots were reported that distinguish between the compaction behavior of powdered material on the basis of their particle size or mixture components. Data required for Heckel analysis are obtained by either out-of-die or in-die methods. The in-die or at-pressure method collects data during the compaction of the powder. On the other hand, the out-of-die or zero-pressure method requires collecting data after the ejection of the compacts, a procedure that eliminates the effect of elastic deformation on the densification of the powder.

The out-of-die Heckel analysis of the compaction of the microemulsion-absorbed granules containing various grades of MCC is shown in FIG. 13. The Heckel plots appear to be linear over the compaction range between 15.6 and 312.3 MPa. Linear regression was performed on the data points of all the powdered materials to calculate the yield strength as previously discussed. Yield strength (see Table 3) increased by increasing the particle size of MCC grades having a 5% moisture content. This may be attributed to the effects of the initial particle size on volume reduction. In addition, absorbing oil into the surface of the powder may alter its compaction properties.

Several other researchers reported that coating the particles of various pharmaceutical powders with layers of surfactant noticeably alters their mechanical behavior when they are compressed into tablets. The degree of coating depends on the available surface area and the absorbing capacity of the powder. Formulations made with Avicel PH-105 had the lowest yield strength at 14.3 MPa (see Table 3). This probably is a result of the smaller particle size of Avicel PH-105, which provides a larger surface area for adsorption. This in turn facilitates homogeneous oil distribution throughout the compact, allows efficient particle lubrication and packing, and mediates plastic deformation. Formulations made with Avicel PH-112 and 113 had the highest yield-strength value among the compacts. Avicel PH-112 and 113 have a moisture content of no more than 1.5% and 2% respectively. The reason for the higher yield-strength value is still unclear. It might be the result of moisture-mediated surface absorption, which limits

the formulations' absorbing capacity. In one reported study, moisture was found to act as a plasticizer and to influence the mechanical properties of MCC. Such a phenomenon might help retain surface characteristics and preserve tableting and compaction properties of adjuvants. The adjuvants, Avicel PH-112 and 113, were added merely to boost the compressibility of the soft oil-absorbed compacts rather than promote oil absorption.

Tableting Performance of the Powdered Self-Emulsified Formulations

To describe the tableting performance of the powdered microemulsion, compressibility, compatibility, and tabletability of the formulations were evaluated.

Compressibility is the ability of a powdered material to undergo a reduction in porosity as a result of applied pressure. This could be represented by a plot of porosity against the applied compaction pressure, as shown in FIG. 14. Compressibility of the powders is an important factor that governs the strength of compacts, especially at lower compaction pressures. This effect is the result of the formation of a larger interparticulate bonding area and a reduction in porosity that arises from plastic deformation. Hence, the more compressible the powder, the stronger the resultant compacts. When the dry powdered microemulsion-based formulations were compressed under the same compression conditions, compacts made with Avicel PH-105 had the lowest porosity and thus were the most compressible among the adsorbed powders. This result might be attributed to the greater plasticity of the formulation containing Avicel PH-105 as indicated by its low yield strength of 14.3 MPa (see Table 3). The outcome also may be the result of the smaller particle size (20 μ m) of Avicel PH-105. Smaller particle size provides larger surface areas for oil adsorption and allows the powder to pack more efficiently. Avicel PH-112 and 113 showed the greatest resistance to plastic deformation at a lower compaction pressure, as observed by their higher yield strengths of 30.9 and 25.1 MPa, respectively (see Table 3). Nevertheless, all the formalities showed great dependence on compression pressure regardless of MCC particle size. The porosity of all powdered materials decreased rapidly with an increase in compaction pressure \leq 120 MPa and reached relatively constant values thereafter.

Compactibility is the ability of a powdered material to produce compacts with sufficient strength under the effect of densification. This can be represented by a plot of tablet tensile strength against the resultant porosity, at which tensile strength decreases exponentially with an increase in porosity, as shown in FIG. 15. This relationship can be expressed by the following equation:

$$\ln \sigma = \ln \sigma_0 - b\epsilon$$

in which σ is the tensile strength, σ_0 is the tensile strength at zero porosity, b is a constant related to the pore distribution in the tablets, and ϵ is the porosity. Tensile strength at zero

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porosity, σ_0 , was obtained by fitting the equation to the data followed by extrapolation. All powdered formulations followed the exponential relationship described in the equation. Tensile strength at zero porosity, σ_0 , (see Table 3) appears independent of the initial MCC particle size. The lowest σ_0 value for compacts made with Avicel PH-105 indicates the weakest bonding, which can be attributed to its highest adsorbing capacity. This causes Avicel PH-105 particles to be fully coated with a film of the oily formulation, thereby reducing the ability for interparticulate interactions and surface bonding.

Tabletability is the ability of a powdered material to produce compacts with sufficient strength under the effect of compaction pressure and is represented by a plot of tablet tensile strength against compression pressure. A linear relationship between tensile strength and compaction pressure was observed for each of the formulations within the compaction range <120 MPa and reached a plateau thereafter, see FIG. 16. The effect of particle size of MCC on tensile strength appears less significant throughout the compaction range. MCC characteristics such as particle size and size distribution were found to have little effect on the tensile strength of tablets made from spray-dried Avicel. This could result from the low MCC loading of 20% in the formulation. The adsorbing capacity of MCC appeared insignificant in terms of producing compacts with distinctive tensile strengths at lower compaction pressures. At compression loads >120 MPa, during which most of the pores are eliminated, the difference in the interparticulate bonding area would be small. At a higher compression pressure, the bonding strength per unit bonding area would be the decisive factor in controlling compact strength. Consequently, Avicel PH-101, 112, and 200 showed the greater tensile strengths of 0.36, 0.39, and 0.34, respectively, at compaction pressures >120 MPa.

Surface Roughness Study

The profile parameters measured for the compacts are listed in Table 4.

TABLE 4

Avicel MCC	P-Profile		W-profile		R-Profile			
	P_s (μm)		W_s (μm)		R_a (μm)		R_z (μm)	
Grade	Upper	Lower	Upper	Lower	Upper	Lower	Upper	Lower
Avicel PH-105	118.2	151.68	391.02	446.9	2.97	1.83	20.07	12.84
Avicel PH-101	123.82	157.09	373.9	486.62	1.84	1.63	12.92	11.6
Avicel PH-113	143.6	144.24	384.26	427.14	1.96	1.84	14.26	13.08
Avicel PH-102	156.78	173.51	386.88	469.76	1.48	1.31	10.62	9.26
Avicel PH-112	152.31	160.58	357.12	405.87	1.85	1.59	13.53	10.91
Avicel PH-200	162.34	175.16	387.62	431.95	1.77	1.52	12.57	11.04

Waviness of the lower surface of the tablets, exposed to the lower punch during compaction, was greater than that of the upper surface of the compacts. This is apparent from the W and P profiles given as W_s and P_s parameters, respectively. Higher values of the W_s parameter for the lower surface of the tablets might be the result of the segregation of the larger granules to the bottom of the die during powder filling. These granules are the Kollidon VA 64-based paste ground with maltodextrin. Segregation was visually evident by the higher degree of mottling of the lower surface caused by the colored granules when compared with the extragranular white MCC powder. However, no change in surface waviness was observed as a function of the initial MCC particle size.

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On the other hand, the P-profile measures both roughness and waviness of the surface. Both granule segregation and MCC particle size induced the P_s parameter, which is a measure of the distance between grooves primarily caused by granules of variable sizes. Higher P_s values of the lower surface of the compacts indicate that surface waviness is the dominant factor in determining the P_s parameter. P_s increased with an increase in particle size from Avicel PH-105 to Avicel PH-200. This is probably because larger-size MCC provides greater spacing between the particles. Because of the powder segregation, the lower punch is exposed to a larger portion of the granules that contain the lipid-based formulation. This in turn provides lubrication to the surface of the punch during tablet compaction and ejection. As a consequence, the roughness profile of the lower surface of the compacts given as R_a and R_z was lower than that of the upper surface of the tablets exposed to the less-lubricated upper punch. However, the MCC particle size was less significant in terms of the roughness parameters. This outcome is attributable to the fact that R_a and R_z are measures of the heights and depths of the peaks and valleys formed on the surface of the tablets as a result of powder compaction. Plastic deformation might have diminished the differences between MCC particles when they were monitored vertically yet maintained their characteristic boundaries detected by the P-profile parameters.

Friability Study

Friability of the compacts made from the powdered self-emulsified system as a function of compaction pressure is shown in FIG. 17. Friability decreased gradually with an increase in compression load and reached a plateau of <0.1% at compression pressures >120 MPa independent of the initial MCC particle size. No effect of MCC grade and size was evident in terms of the friability of the compacts. This correlates well with the compressibility and tabletability data. Porosities and tensile strengths for all the preparations

reached their optimum values at 120 MPa, reflecting the greatest interparticulate bonding that was further induced by oil bridging the particles

Dissolution Study

To evaluate the emulsion release from the absorbing compacts, dissolution studies were performed for tablets prepared at a low compaction pressure of 31.2 MPa. Ideally, SNEDDS should be released from the tablets and completely emulsify into the dissolution medium. This effect was evaluated by measuring the cumulative percent of the drug solubilized into the aqueous medium as part of the released emulsion. Dissolution plots of the self-emulsified tablets are shown in FIG. 18. The dissolution rate within the first 45 min appeared to be dependent on MCC particle size. The cumulative percent of

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CoQ₁₀ solubilized in 45 min for compacts made with Avicel PH-200, 102, 112, 113, 101 and 105 was 51.5, 49, 44, 39.5, 36, and 8.7%, respectively. After 1 hour, dissolution reached a plateau with an average release of 55% (except for Avicel PH-105). Poor CoQ₁₀ dissolution might be the result of an irreversible hydrophobic interaction between CoQ₁₀ and MCC. Initial powder compaction and slow disintegration (see Table 3) also might have induced irreversible surface adsorption to the soluble excipients of the formulation. This process causes variable release rates. Oily components of the formulation are emulsified into the aqueous medium at a faster rate compared with the release of CoQ₁₀. However, tablets made with Avicel PH-105 induced sustained release of CoQ₁₀ in a time span of 6 hours. As previously discussed, tablets made with Avicel PH-105 had the least yield and tensile strength and the lengthiest disintegration time (see Table 3). This suggests oil-induced bridging and sticking between the Avicel particles, an outcome that provides a greater area of contact. The increase in the cohesion between the particles accounts for delayed release rates without increasing the hardness of the tablets.

Although the present invention has been disclosed in terms of a preferred embodiment, it will be understood that numerous additional modifications and variations could be made thereto without departing from the scope of the invention as defined by the following claims.

What is claimed is:

1. An orally administered dietary supplement including a eutectic-based delivery system, comprising:

a) ubiquinone; and

b) a sufficient amount of a volatile essential oil to solubilize the ubiquinone, and wherein said volatile essential oil is present in a sufficient amount to reduce the melting point of ubiquinone to 37° C. or below, and thereby solubilize the ubiquinone comprised in the orally administered dietary supplement at or below body temperature.

2. The orally administered dietary supplement of claim 1, wherein said volatile essential oil is selected from the group consisting of menthol, spearmint oil, peppermint oil, lemon oil, anise oil, and mixtures thereof.

3. The orally administered dietary supplement of claim 1, further comprising a surfactant.

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4. A delivery system for pharmacologically effective agents, comprising:

a) ubiquinone;

b) a surfactant;

c) a sufficient amount of a volatile essential oil to reduce the melting point of ubiquinone to 37° C. or below, and thereby solubilize the ubiquinone comprised in the delivery system at or below body temperature.

5. The eutectic-based delivery system of claim 4, wherein said volatile essential oil is selected from the group consisting of menthol, spearmint oil, peppermint oil, lemon oil, anise oil, and mixtures thereof.

6. The eutectic-based delivery system of claim 5, wherein said essential oil is lemon oil.

7. The eutectic-based delivery system of claim 4, wherein said surfactant is polyoxyl 35 castor oil or a medium chain mono- and diglyceride.

8. The orally administered dietary supplement of claim 1, wherein the dietary supplement composition is contained in a capsule.

9. The eutectic-based delivery system of claim 4, wherein the delivery system is contained in a capsule.

10. An orally administered dietary supplement including a eutectic-based delivery system, comprising

a) ubiquinone; and

b) a sufficient amount of a volatile essential oil to solubilize the ubiquinone, and wherein said volatile essential oil is present in a sufficient amount to reduce the melting point of ubiquinone to 37° C. or below, and thereby solubilize the ubiquinone comprised in the orally administered dietary supplement at or below body temperature; and

c) wherein the dietary supplement composition is contained within a capsule.

11. The orally administered dietary supplement of claim 10, wherein the capsule is a hard capsule.

12. The orally administered dietary supplement of claim 10, wherein the capsule is a soft capsule.

13. The orally administered dietary supplement of claim 1, wherein the amount of the volatile essential oil is sufficient to solubilize the ubiquinone after ingestion by a patient.

* * * * *

CERTIFICATE OF SERVICE

I hereby certify, that on January 10, 2014, a true and correct copy of the Principal Brief of Plaintiff-Appellant Jarrow Formulas, Inc. was caused to be served on the below-listed counsel by CM/ECF and electronic mail (by agreement of counsel):

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CERTIFICATE OF COMPLIANCE

1. This brief complies with the type-volume limitation of Federal Rule of Appellate Procedure 32(a)(7)(B). The brief contains 13,491 words, excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(a)(7)(B)(iii).
2. This brief complies with the typeface requirements of Federal Rule of Appellate Procedure 32(a)(5) and the type style requirements of Federal Rule of Appellate Procedure 32(a)(6). The brief has been prepared in a proportionally spaced typeface using MS Word in a 14 point Times New Roman font.

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